

Integer and fractional order models for rabies: a theoretical approach

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Abstract : The rabies virus usually transmits either from animal to man or animal to animal or human to human as the case may be but the major transmitters of the virus are dogs globally. In this work, an integer order SEIR epidemic model was formulated to quantify and give an insight into the spread of rabies within the dog population. The integer order model was studied qualitatively and its results were obtained theoretically before it was modified into the non-integer order counterpart to cater for the data agreement deficiency associated with the integer order epidemic models. As rabies prevalence varies from localities to localities, the theoretical outcomes of the analysis could reveal the genuine picture of rabies dynamics in a particular locality if the actual rabies data of the locality is available.

Keywords : Rabies; Integer order; Model; Fractional order

2010 Mathematics Subject Classification: 92B05, 92D30, 34D20, 34A08

Receive: 17 October 2021, **Accepted:** 1 February 2022

1 Introduction

Rabies is a deadly infection that affects mammals, triggered by a virus. While rabies is preventable, it is prevalent in numerous populations of warm-blooded animals [30]. Rabies exists in over 150 nations and regions worldwide and over 55 000 individuals die of the rabies yearly [14, 34]. The most reported cases of rabies exist in wild animals such as bats, skunks, raccoons and foxes [2]. Rabies also spread among domestic animals. In fact, dogs remain the major agents in the transmission of rabies virus from animal to man [29]. The rabies is spread through contact with the saliva of infected animals via scratches or bite [18]. Infected animals produce a considerable quantity of virus in their saliva. After a man is attacked by an infected agent, the virus moves into the nervous system and pass through the nerves to the brain where it duplicates and the symptoms begin to appear [11]. The salivary gland is infected as soon as the virus duplicates and the saliva becomes the major channel of transmission of the virus [10].

The rabies virus has an incubation period that varies from a few days to some years but usually, it falls within one to three months [36]. However, the period is a function of the circumstances such as parts of the body pricked and the degree of the bite. Generally, the incubation for multiple bites, severe wounds and bites around the head is shorter. On the other hand, a single bite in the region below the waist and wounds of lower degree is associated with prolonging incubation period [31]. The early symptoms and signs of rabies attack in man include; fever, pain, headache, numbness or burning at the region of the wound and general body weakness [12]. Severe symptoms and signs include cerebral dysfunction, confusion, partial paralysis, anxiety, agitation, insomnia, paranoia, abnormal behaviour, hallucinations, terror and delirium [36, 21]. At the advanced stage, the infected individual begins to secrete an enormous quantity of tear

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and saliva, develops hydrophobia and inability to communicate. Death, usually, follows those signs and symptoms within a few days [1].

Generally, methods for checking dog rabies are many but the commonest ones include the management of dog population, the restriction of dog movement and dog vaccination [28]. However, dog vaccination remains the best control measure of rabies globally [25]. Currently, rabies spreads in regions where extensive dog vaccination programmes are yet to be launched. To date, rabies has no cure once the symptoms and signs have developed [22]. However, if an individual has been infected with rabies but the symptoms are yet to be developed then there exists an adequate post-exposure remedy for the individual. Post-Exposure Prophylaxis (PEP) therapy involves the application of vaccination to stop the virus from getting into the human brain [36]. Despite the adequacy of PEP, thousands of individuals still die of rabies virus since PEP is costly and inaccessible in most rabies endemic regions [32].

A good number of models that are related to the analysis of rabies have been advanced over the years. For instance, [37] investigated the factors that were responsible for poor compliance with the WHO recommendation of PEP agenda in Tanzania. They quantified the coping strategies, health-seeking attitude, household cost, and outcome of contact with the rabies virus in urban and rural communities in Tanzania. Their estimations indicated that a typical patient in a rural community in Tanzania, where the vast majority of people live below the poverty line, would have to spend more than 100 US dollar to meet up with the WHO recommendation for PEP schedule. They, therefore, concluded that high costs and regular shortage of PEP accounted for poor adherence to PEP regimes in Tanzania.

Also, [?] adopted SEIR epidemic model to investigate the necessity of pre-exposure vaccination in man and its effect on the transmission of rabies virus from animals to man. The result obtained from the analysis showed that implementation of pre-exposure vaccination for man prevented a good number of susceptible individuals from contracting rabies virus. As a control strategy, in addition to dog vaccination and culling, the author recommended the implementation of pre-exposure vaccination of rabies for man particularly the higher-risk individuals such as veterinary students, veterinary technicians, laboratory workers, veterinarians and control officers for animals so as to reduce the transmission of the virus.

[16] also formulated an SEIR model incorporating vaccination to study the transmission dynamics of dog rabies in Bolgatanga district in Ghana. They obtained a numerical value of 0.3755 for R_0 which indicated non-endemicity and used a herd immunity threshold to show that rabies eradication in Bolgatanga district was a function of vaccination coverage of not less than 75.37% of the entire dog population. In the same vein, a model which was based on the vaccination of dog population as a means of curbing rabies transmission in Addis Ababa was developed in [18]. The researchers discovered that while pre-exposure prophylaxis (PrEP) was indispensable in preventing the susceptible individuals from contracting rabies virus, it could not avert future transmission of rabies. Besides, the simulated results of the R_0 showed that dog population management, stray dog culling and dog vaccination were the best approach to curb rabies spread in Addis Ababa.

Mathematical models present a comparatively inexpensive means to investigate the spread and control of epidemic diseases [24]. Once a model is developed, the solutions offer anticipation concerning the prospect of the disease which assists to forecast whether the disease develops into an epidemic or not ([26], [39]). Differential calculus plays a significant role in the development of epidemic models. With the exception of the work of [14], most known rabies models are formulated in terms of the integer-order ordinary differential equations [35, 4, 40, 38, 9, 23, 5]. While the solutions of the integer-order models enable us to envisage the mode of the transmission of diseases, the solutions do not always agree with the data collected. Fractional order models are advanced to overcome the shortcoming of data agreement in integer-order models ([14], [6], [27]).

In this work, we first introduce an SEIR integer-order mathematical model for the spread of rabies in the dog population and study the stability of the solutions of the model. Then, we transformed the model to the fractional-order.

2 The Integer Order Model

To develop a model that explains the dynamics of rabies in the dog population, an SEIR compartmental model is adopted to decompose the entire population into different groups according to their epidemiological status. The following notations are used for the variables.

$N(t)$: The total population of dogs at time t .

$S(t)$: The entire population of susceptible dogs at time t .

$E(t)$: Population of exposed dogs at time t .

$I(t)$: The total population of infected dogs at time t .

$R(t)$: Population of recovered dogs at time t .

Clearly,

$$N(t) = S(t) + E(t) + I(t) + R(t)$$

for all time t . The transmission diagram for the dynamics is illustrated in Figure 1. The model is built on the ground that rabies is a deadly disease for dogs and the best way to avert the mortality due to rabies is to employ vaccination (PrEP and PEP) to the susceptible and the exposed dogs. It is assumed that the coverage of PEP is higher than PrEP i.e. $v_2 > v_1$. Also, both vaccines do not confer permanent immunity. It is also assumed that all infective animals die either naturally or by culling and there is no tendency for an infective animal to recover from infectiousness. Following these assumptions, we offer the following set of integer order ordinary differential equations:

$$\frac{dS}{dt} = \pi - \beta SI - \mu S - v_1 S + \alpha R \quad (2.1)$$

$$\frac{dE}{dt} = \beta SI - v_2 E - \sigma E - \mu E \quad (2.2)$$

$$\frac{dI}{dt} = \sigma E - \mu I - \varepsilon I \quad (2.3)$$

$$\frac{dR}{dt} = v_1 S + v_2 E - \alpha R - \mu R \quad (2.4)$$

where:

π : recruitment rate of dogs

β : effective contact rate

v_1 : vaccination rate before exposure

v_2 : vaccination rate after exposure

α : waning rate of immunity

σ : progression rate into infectiousness

ε : rate of culling

μ : natural mortality rate

The sum of (2.1)-(2.4) yields

$$\begin{aligned} \frac{dN}{dt} &= \pi - \mu(S(t) + E(t) + I(t) + R(t)) - \varepsilon I \\ \Rightarrow \frac{dN}{dt} &< \pi - \mu(S(t) + E(t) + I(t) + R(t)) \end{aligned} \quad (2.5)$$

Taking the limit supremum of (2.5)

$$\lim_{t \rightarrow \infty} \text{Sup}(S(t) + E(t) + I(t) + R(t)) < \frac{\pi}{\mu} \quad (2.6)$$

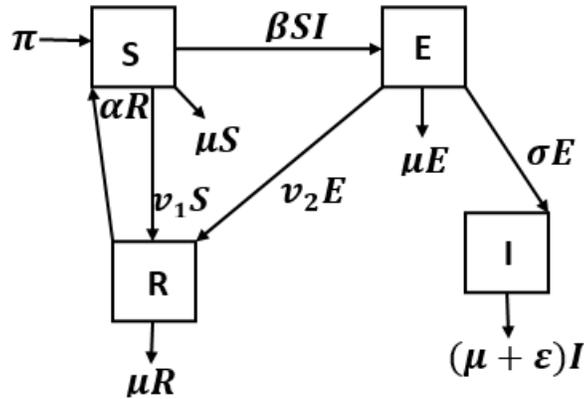


Figure 1: Transmission diagram of the model.

The implication of (2.6) is that the solutions to the system are bounded in the region given by

$$\Gamma = \left\{ (S, E, I, R) : 0 < S + E + I + R \leq \frac{\pi}{\mu} \right\} \quad (2.7)$$

Hence, the analysis of the model can be considered in the region defined by Γ .

2.1 Existence of the disease-free equilibrium (DFE)

When the rabies virus is virtually non-existence in the animal population, there is neither exposed nor infected dogs. However, there exists recovered compartment due to the presence of PrEP but the waning rate immunity parameter is assumed to be zero since the animal population is free from the rabies virus. Based on this, the DFE is obtained as

$$E_0 = \left(\frac{\pi}{(\mu + v_1)}, 0, 0, \frac{\pi}{(\mu + \alpha)(\mu + v_1)} \right) \quad (2.8)$$

2.2 Existence of endemic equilibrium (EE)

When the rabies virus is prevalent in the animal population, the endemic equilibrium $E_* = (S_*, E_*, I_*, R_*)$ is obtained as

$$\left. \begin{aligned} S_* &= \frac{d_1 d_2}{\sigma \beta} \\ E_* &= \frac{1}{\sigma \beta d_2 d_3} [\pi \sigma \beta d_3 + \alpha v_1 d_1 d_2 + \alpha \sigma \beta v_2 d_1 - d_1 d_2 d_4] \\ I_* &= \frac{1}{\beta d_1 d_2 d_3} [\pi \sigma \beta d_3 + \alpha v_1 d_1 d_2 + \alpha \sigma \beta v_2 d_1 - d_1 d_2 d_4] \\ R_* &= \frac{d_1 (v_1 d_2 + v_2 \sigma \beta)}{\sigma \beta d_3} \end{aligned} \right\} \quad (2.9)$$

where

$$\left. \begin{aligned} d_1 &= \mu + \varepsilon \\ d_2 &= v_2 + \mu + \sigma \\ d_3 &= \mu + \alpha \\ d_4 &= \mu + v_1 \end{aligned} \right\} \quad (2.10)$$

2.3 The reproduction number (R_o)

The question of whether rabies will spread in the animal population or not can be answered by the numerical value of a threshold quantity termed the basic reproduction number. Following the approach adopted in [7], the basic reproduction number is obtained as

$$R_o = \left(\frac{\pi}{(\mu + \varepsilon)(\mu + v_1)(\mu + \sigma + v_2)} \right) \quad (2.11)$$

2.4 Stability analysis of the DFE

The stability status of the model shall be examined around the DFE via variational matrix. The variational matrix conforming to the model with respect to (2.8) is given as

$$J(E_0) = \begin{pmatrix} -(\mu + v_1) & 0 & -\frac{\pi\beta}{(\mu+v_1)} & \alpha \\ 0 & -(v_2 + \mu + \sigma) & \frac{\pi\beta}{(\mu+v_1)} & 0 \\ 0 & \sigma & -(\mu + \varepsilon) & 0 \\ v_1 & v_2 & 0 & -(\mu + \alpha) \end{pmatrix} \quad (2.12)$$

The characteristic equation of (2.12) is evaluated as

$$(\lambda + d_4)(\lambda + d_3)[(\lambda + d_1)(\lambda + d_2) - d_5] - \alpha v_1[(\lambda + d_1)(\lambda + d_2) - d_5] = 0 \quad (2.13)$$

where:

$$d_5 = \frac{\pi\beta}{\mu + v_1} \quad (2.14)$$

Already, d_1, \dots, d_4 have been defined in (2.10)

Eqn. (2.13) is expanded to

$$p_0\lambda^4 + p_1\lambda^3 + p_2\lambda^2 + p_3\lambda + p_4 = 0, \quad (2.15)$$

where:

$$\begin{aligned} p_0 &= 1, \\ p_1 &= d_1 + d_2 + d_3 + d_4, \\ p_2 &= d_1d_2 - d_5 + (d_1 + d_2)(d_3 + d_4) + d_3d_4 - \alpha v_1, \\ p_3 &= (d_3 + d_4)[d_1d_2 - d_5] + (d_1 + d_2)[d_3d_4 - \alpha v_1], \\ p_4 &= d_1d_2d_3d_4 + \alpha v_1d_5 - d_3d_4d_5 - \alpha v_1d_1d_2. \end{aligned}$$

Obviously, p_0 and p_1 are positive. Following Routh-Hurwitz stability criteria outlined in [8], the DFE of the model is locally asymptotically stable if

$$p_1 > 0, p_3 > 0, p_4 > 0 \quad \text{and} \quad p_1p_2p_3 > p_3^2 + p_1^2p_4 \quad (2.16)$$

3 The Fractional Order Model

Of recent, mathematical models designed in terms of non-integer order ordinary differential equations have appeared to be in good agreement with true data in engineering, biology and physics ([33], [3], [13]). As a result of this, a good number of models have been transformed to non-integer order ([19], [17], [20]). However, most of the recent modifications are based on the Caputo differential equations owing to the complexities in describing the initial conditions for the differential equations of Riemann Liouville type. According to [14], given a function $f : R^+ \rightarrow R$, the Riemann Liouville integral of order $\alpha > 0$ is defined as

$$I^\alpha f(t) = \frac{1}{\Gamma\alpha} \int_0^t (t - \tau)^{\alpha-1} f(\tau) d\tau \quad (3.1)$$

while the Caputo non-integer order derivative of order $\alpha \in (n - 1, n)$ of $f(t)$ is defined as

$$D^\alpha f(t) = I^{n-\alpha} D^n f(t) \quad (3.2)$$

In (3.2), $n - 1$ is the integer part of α and $D = \frac{d}{dt}$.

The major distinction between the integer-order mathematical models and the non-integer extensions is just the exponent of the equations. However, Diethelm employed a straightforward dimension analysis to transform the integer-order model and then modify the order of the transformed model into a real number [15]. In the system (2.1)-(2.4), the RHS of the model is measured in terms of time [i.e. $(time)^{-1}$]. Hence, when the order of the model is changed to α then, the LHS of the model would have to be measured in $(time)^{-\alpha}$. Therefore, to maintain the balance in the dimensions of the system, the parameters of the model shall have their dimensions changed and the model finally becomes

$$\left. \begin{aligned} D^\alpha S &= \pi^\alpha - \beta^\alpha SI - \mu^\alpha S - v_1^\alpha S + \alpha^\alpha R \\ D^\alpha E &= \beta^\alpha SI - \mu^\alpha E - \sigma^\alpha E - v_2^\alpha E \\ D^\alpha I &= \sigma^\alpha E - \mu^\alpha I - \varepsilon^\alpha I \\ D^\alpha R &= v_1^\alpha S + v_2^\alpha E - \mu^\alpha R - \alpha^\alpha R \end{aligned} \right\} \quad (3.3)$$

where $0 < \alpha \leq 1$.

Generally, the system (3.3) can be condensed to the system (2.1)-(2.4) if the order $\alpha \rightarrow 1$. Also, the solutions of the system (3.3) can be obtained numerically with the help of mathematical software if the real data for the variables and the parameters of the model are available.

4 Discussion of Results

The result obtained for the reproduction number in (2.11) showed that the extensive vaccination programmes (v_1 and v_2), as well as adequate culling, were capable of reducing rabies spread and transmission in the animal population. In the same vein, the conditions for achieving the stability of the disease-free equilibrium were derived in (2.16). The stability of the disease-free equilibrium implied that rabies spread and transmission would fail in the animal population even if a rabid dog was introduced into the population.

However, the entire analysis was qualitative in nature while the quantitative aspect was omitted due to the unavailability of real data. It is hoped that the theoretical results of the study will provide a necessary framework for the assessment of rabies management in any part of the world. As rabies incidence differs from regions to regions, the true picture of rabies dynamics in a particular region can be revealed from our theoretical results if the real rabies data of the region is available. Besides, the behaviour of the

integer-order and the fractional-order models [i.e. system (2.1)-(2.4) and system (3.3)] can be compared with the aids of mathematical software (Maple or Mathematica) if there is the availability of real data for the variables and parameters of the model.

5 Conclusion

In this work, an integer-order ordinary differential equation was formulated to quantify the transmission dynamics of rabies virus in dog population. The equilibrium analysis of the model was performed and both the disease-free and the endemic equilibria of the model were obtained. The reproduction number of the model was also derived and the conditions for the stability of the disease-free equilibrium of the model were established. The integer-order model was later transformed into the fractional-order via Caputo derivative and the numerical analysis to compare the two systems [model (2.1)-(2.4) and model (3.3)] was left to be performed in the nearest future.

Acknowledgement(s): I would like to thank the handling editor and the referee(s) for their comments and suggestions on the manuscript.

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