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Assessing the population transmission dynamics of tilapia lake virus in farmed tilapia

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Abstract

A novel virus, tilapia lake virus (TiLV), has been identified as a key pathogen responsible for disease outbreak and mass mortality of farmed tilapia. We used a deterministic susceptible-infectious-mortality (SIM) model to derive key disease information appraised with published TiLV-induced cumulative mortality data. The relationship between tilapia mortality and TiLV exposure dosages was described by the Hill model. Furthermore, a disease control model was proposed to determine the status of controlled TiLV infection using a parsimonious control reproduction number (R_C)-control line criterion. Results showed that the key disease determinants of transmission rate and basic reproduction number (R_0) could be derived. The median R_0 estimate was 2.59 in a cohabitation setting with 2.6×10^5 TCID50 fish^{-1} TiLV. The present R_C-control model can be employed to determine whether TiLV containment is feasible in an outbreak farm by quantifying the current level of transmission. The SIM model can then be applied to predict what additional control is required to manage $R_C < 1$. We offer valuable tools for aquaculture engineers and public health scientists the mechanistic-based assessment that allows a more rigorous evaluation of different control strategies to reduce waterborne diseases in aquaculture farming systems.

KEYWORDS
disease transmission dynamics, modelling, tilapia, tilapia lake virus (TiLV)

1 | INTRODUCTION

Tilapines, serving as the main protein source in the world, are essential to global and domestic fishery industries (FAO, 2004, 2010a, 2010b). As the second most important farmed fish worldwide, the annual production of tilapines is documented to be >3.9 million tons in 2015 (FAO, 2010a, 2010b, 2017b). On the other hand, various pathogens including bacteria, fungi, protozoa and virus have been reported as the major threats to tilapine aquaculture (Abowei, Briyai, & Bassey, 2011; Bigarré, Cabon, & Baud, 2009; Popma & Masser, 1999). While bacterial and fungal infections are mostly alleviated through antibiotics treatments, little is known for therapy and containment strategies for waterborne and water-related viral infections of tilapia (Sommerset, Krossøy, Biering, & Frost, 2005).

Tilapia lake virus (TiLV) disease, also known as syncytial hepatitis of tilapia (SHT), is a novel infectious disease caused by an orthomyxo-like virus that contributes to substantial mortalities in farmed tilapia. The TiLV was firstly identified in farmed and wild-lived tilapia in Israel (Eyngor, Zamostiano, & Kembou Tsofack, 2014). Most recently, TiLV outbreaks were reported in Ecuador, Thailand, Egypt, Colombia and Taiwan (Bacharach et al., 2016; Bureau of Animal and Plant Health Inspection and Quarantine, 2017; Fathi et al., 2017; Kembou Tsofack et al., 2016; Surachetpong et al., 2017).

The first-ever epidemic disease of TiLV has intensified the risk of global fishery industry, resulting in mortality levels ranging from 9.2% to 90% in Egypt, Israel, Thailand and Ecuador (Eyngor et al., 2014; Fathi et al., 2017; Ferguson et al., 2014; Jansen & Mohan, 2017; Surachetpong et al., 2017). The route of TiLV transmission was evidenced to be through waterborne and horizontal (Eyngor et al., 2014; Tattiyapong, Dachavichitlead, & Surachetpong, 2017). Furthermore, a recent study demonstrated that TiLV could persist up to 12–14 days postinfection (dpi) in mucus, liver and intestines of

cohabiting fish (Liamnimitr, Thammatorn, Uthoomporn, Tattiyapong, & Surachetpong, 2018), indicating that global aquaculture system could be undermined with TiLV infections if outbreaks are not effectively controlled.

Among more than 100 tilapia species, Nile tilapia (*Oreochromis niloticus*) is the predominant farmed species in the world (FAO, 2010b). It was also evidenced that TiLV-affected farmed species were hybrid tilapia (*O. niloticus* × *O. aureus*) in Israel, Nile tilapia (*O. niloticus*) in Egypt, Ecuador and Thailand (Dong et al., 2017; Eyngor et al., 2014; Fathi et al., 2017; Ferguson et al., 2014; Surachetpong et al., 2017), and Red tilapia in Thailand (Dong et al., 2017; Surachetpong et al., 2017).

The unprecedented TiLV outbreak in Taiwan in June 2017 inspired us to assess the mechanistic relationship between virus dosage and TiLV-induced mortality and to synthesize the associated key disease information to understand transmission dynamics. The integration of mathematical model and disease processes within aquatic animal populations in this study can provide tactic tools to evaluate impacts of emerging diseases and develop mitigation measures. To our knowledge, this is the first mechanistic modelling approach that accounts for the transmission dynamics of TiLV in a tilapia farming system. Therefore, the purposes of this study were threefold: (a) to assess the relationship between cumulative mortality and TiLV exposure doses in tilapia, (b) to explore population transmission dynamics of TiLV in tilapia and (c) to estimate threshold population size and to provide control strategies for preventing TiLV outbreaks.

2 | MATERIALS AND METHODS

2.1 | Study data

The epidemiological literature quantifying the relationship between TiLV-induced mortality and key disease determinants is limited. Thus, we restricted our quantitative analysis to available literature accounting for the experimental scale systems.

Bioassays of cumulative mortalities of TiLV-challenged tilapia were adapted from the previous studies (Eyngor et al., 2014; Tattiyapong et al., 2017). In brief, Nile tilapia was exposed to TiLV via intraperitoneally (I.P.) injection or cohabitation route (Eyngor et al., 2014; Tattiyapong et al., 2017) (Figure 1a,b; Supporting Information Figure S1, Tables S1 and S2). For exposure route of I.P. injection, fish weighing from 30 to 35 g were injected with supernatant from E-11 cells infected with TiLV at a dose of 2.6×10^5 or 1×10^6 50% tissue culture infective dose (TCID50) per fish, whereas in control groups were injected with uninfected E-11 cell cultures (Eyngor et al., 2014; Tattiyapong et al., 2017).

For exposure route of cohabitation, groups of 30 Nile tilapia were kept in 200 L aquariums divided into three compartments by water-permeable grids that allowed water circulation throughout the aquariums (Eyngor et al., 2014) (Supporting Information Figure S1). The control group ($n = 30$) was kept in the middle compartment of aquarium, whereas fish surviving from I.P. infection trials were pooled and divided into the other two compartments (each with 15 fish) and infected once again by I.P. injection (Eyngor et al., 2014) (Supporting Information Figure S1).

2.2 | Susceptible-infectious-mortality model

The population dynamics of TiLV-induced disease transmission for tilapia under treatment of cohabitation can be described by a deterministic three-compartmental SIM model (Figure 1c). The dynamics of three categorized compartments can be described mechanistically as Equations 1–3 (Table 1) where *S*, *I* and *M* represent populations in susceptible, infected and mortality states for aquaculture species exposed to TiLV, respectively, β is the transmission rate (day^{-1}), and α is the mortality rate (day^{-1}). Two key transmission parameters α and β in SIM model can be estimated based on the published cumulative mortality data. The *S*, *I* and *M* population dynamics were simulated in unit fraction.

After obtaining β and α, the basic reproduction number (R_0) can be determined using Equation 4 (Table 1) (Anderson & May, 1991) where N_0(–) is the initial host population size of Nile tilapia. R_0 can be used to characterize the critical components involved in TiLV-tilapia transmission dynamics. R_0 quantitatively characterizes the average number of new fish infected by a fish with TiLV in an entirely susceptible population.

R_0 can also be taken proportional to total number or density of hosts that are subject to TiLV infections as Equation 4 where N(–) and N_T(–) are host population and threshold population sizes of Nile tilapia, respectively. If N is below threshold magnitude ($N < N_T$), the pathogen cannot spread, and essentially no fish is infected, that is, $I = 0$ (Anderson & May, 1991). On the other hand, the N_T and force of infection (λ_F, day^{-1}) can also be estimated by applying Equations 5 and 6, respectively (Table 1) (Anderson & May, 1991).

2.3 | Dose–response modelling

We constructed the cumulative mortality–TiLV exposure dosage relationship by fitting a two-parameter Hill model to related published studies (Eyngor et al., 2014; Tattiyapong et al., 2017) (Figure 1c). In fitting the Hill model to the observed datasets, the cumulative mortality–TiLV exposure dosage profile can be expressed as Equation 7 (Table 1) where $L(D)$ is the cumulative mortality to specific exposure dose, D (TCID50), LD50 is the exposure dose causing 50% of the cumulative mortality, and n is the fitted Hill coefficient. Hill coefficient $n = 1$ represents a linear response fashioned as the Michaelis-Menton mode, and $n > 1$ represents a sigmoidal response that is ultrasensitive to the pathogen toxicities.

2.4 | Disease control model

In this study, we used the control reproduction number R_C (the average number of new fish infected by a fish with TiLV given current control measures) to provide a theoretically sound measure to assure controlled TiLV infection.

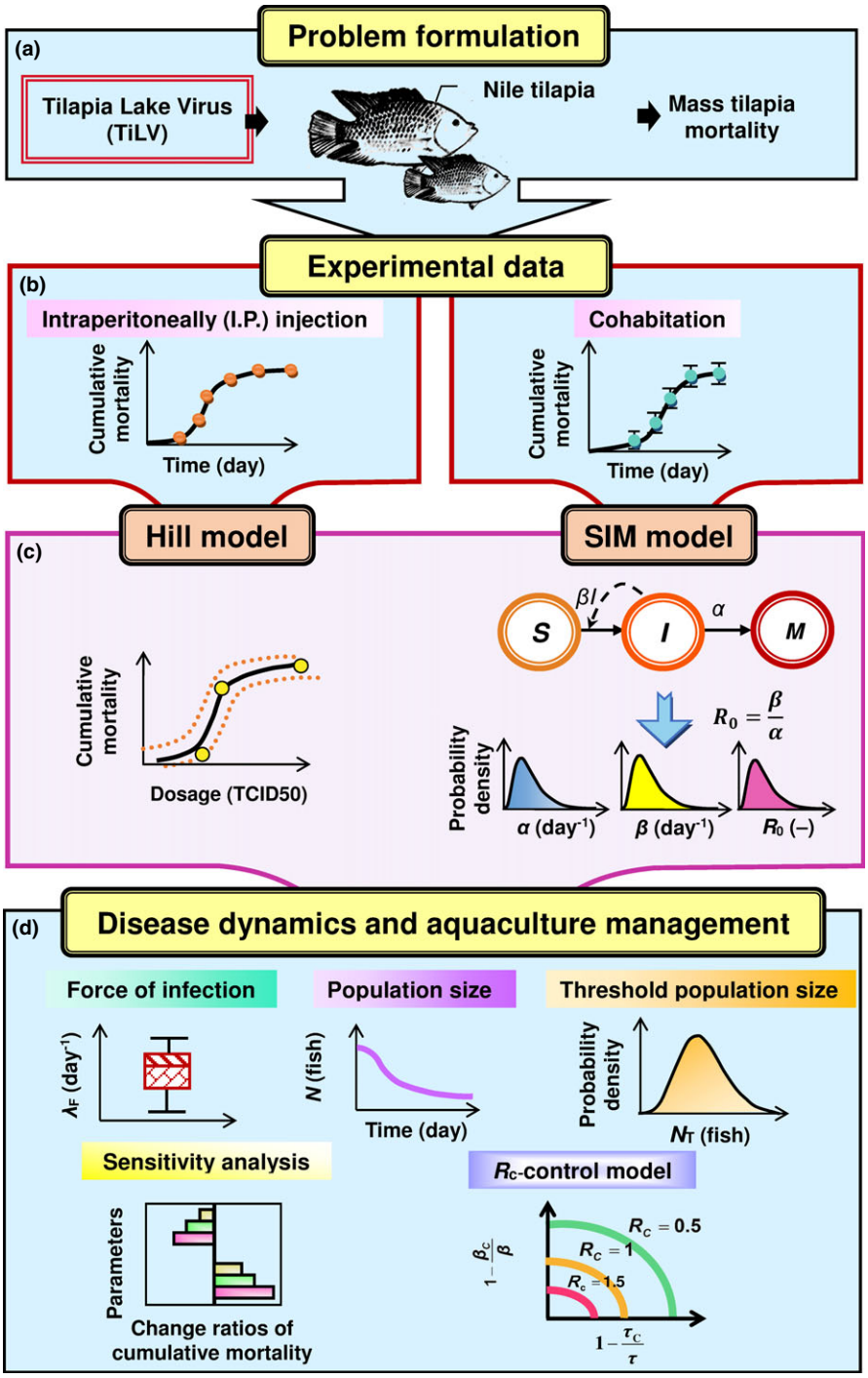

FIGURE 1 Schematic showing the framework of (a) experimental data of tilapia subjected to tilapia lake virus (TiLV) via routes of intraperitoneally (I.P.) injection and cohabitation, (b) experimental data-based TiLV toxicity assessment, (c) epidemiological modelling and (d) disease dynamics and aquaculture management strategies for TiLV containment

However, there are practical limitations existing in a real farming system: R_C can only be derived from the SIM model with local information and cannot be measured directly in the field. To overcome these predicaments, we propose a disease control model in determining the status of controlled TiLV infection. The R_C-control model only requires fish population size-related data. The approach employs a parsimonious R_C-control line criterion and is described as follows.

The contour plots of R_C were schematized based on Equations 8 and 9 (Table 1; Figure 1d). In Equation 8, τ is the infection time (day) that is reversely proportional to the estimated TiLV mortality rate (α), β_C and τ_C are controlled transmission rate and infection time, respectively. On the other hand, in Equation 9, N_0 is the initial population size of Nile tilapia, N_T is the estimated threshold population size, and n_C and N_C are controlled population and threshold population sizes, respectively.

In view of the control lines of reductions in infection time (D) – transmission rate (β) and threshold population size (N_T) – population size (N), if a given infectious agent is contained in the contour lines of $R_C < 1$, the outbreak is controlled eventually. In regions of $R_C > 1$, additional control measures should be intervened to prevent spread of TiLV in tilapia ponds.

TABLE 1 Equations for susceptible-infectious-mortality (SIM), epidemiological, dose–response and disease control models used in this study (see text for the symbol meanings)

Equations	
Susceptible-infectious-mortality (SIM) model	
$\frac{dS}{dt} = -\beta SI$	(1)
$\frac{dI}{dt} = \beta SI - \alpha I$	(2)
$\frac{dM}{dt} = \alpha I$	(3)
Epidemiological model	
$R_0 = \frac{N_0\beta}{\alpha} = \frac{N}{N_T}$	(4)
$N_T = \frac{\alpha}{\beta}$	(5)
$\lambda_F = \beta M$	(6)
Dose–response model	
$L(D) = \frac{100^n}{LD50^n + D^n}$	(7)
Disease control model	
$R_C = R_0 \times \frac{\beta_C}{\beta} \times \frac{\tau_C}{\tau}$	(8)
$R_C = R_0 \times \frac{n_C}{N_0} \times \frac{N_T}{N_C}$	(9)

2.5 | Model calibration

The SIM model was applied to cumulative mortality data to derive estimates of β and α for Nile tilapia posed by 2.6×10^5 TCID50 fish^{-1} TiLV under treatment of cohabitation. Equations 1–3 were applied to fit the cumulative mortality curves. The R_0 estimate can then be obtained by incorporating the epidemiological models of Equation 4 (Table 1). The standard metrics used to assess performance of the SIM model and validate simulations with the published experimental data was root-mean-square error (RMSE) as

$$\text{RMSE}\,(\%) = \sqrt{\sum_{i=1}^{N} \frac{(A_i - F_i)^2}{N}}$$

where N represents the number of observations, A_i represent values of experimental data and F_i are values from simulation.

2.6 | Uncertainty and sensitivity analyses

We implemented the Monte Carlo (MC) analysis to obtain 2.5 and 97.5 percentiles as the 95% confidence interval (CI) for quantifying uncertainties of parameter estimates. We performed the MC simulations with 10,000 iterations for robust value estimations. We employed the Crystal Ball software (version 2000.2, Decisioneering, Inc., Denver, CO, USA) to implement the MC simulation.

We used TableCurve 2D (version 5.01, AISN Software, Mapleton, OR, USA) to fit related published data for describing profiles of R_0–exposure duration relationships. We performed simulations of the SIM model by Berkeley Madonna 8.0.1 (Berkeley Mandonna was developed by Robert Macey and George Oster of the University of California at Berkeley). We also performed a sensitivity analysis to identify the most significant parameters subject to the changes of cumulative mortality (Figure 1d).

3 | RESULTS

3.1 | Cumulative mortality of Nile tilapia-infected with TiLV via IP injection

The relationship between cumulative mortality (%) and exposure doses (TCID50) of TiLV via I.P. injection can be well expressed as a Hill-based dose–response profile (Figure 2). The estimated exposure dose causing half of Nile tilapia mortality via I.P. injection was 5.7×10^4 TCID50 with a fitted Hill coefficient $n = 0.65$ ($r^2 = 0.99$, $p < 0.001$).

3.2 | Host susceptibility and disease dynamics via cohabitation

We estimated α, β, R_0 and N_T for Nile tilapia infected with 2.6×10^5 TCID50 fish^{-1} TiLV via cohabitation by fitting a deterministic SIM model to the cumulative mortality data (Eyngor et al., 2014) (Supporting Information Figure S1). The estimate of R_0 is 2.60 ± 0.16 (mean ± *SD*), implicating that the epidemic of TiLV was spreading within tilapia population via cohabitation route and the incidence was increasing.

Moreover, to estimate key epidemiological parameters of TiLV transmission in probability distributions, a lognormal (LN) probability model can best-fit ($r^2 = 0.99$) to describe α, β, R_0 and N_T estimates. Geometric mean (GM) and geometric standard deviation (GSD) are used to characterize a LN distribution. The GMs of α, β and R_0 are 0.44, 1.13 day^{-1} and 2.59 with GSDs of 1.06, 1.01 and 1.03,

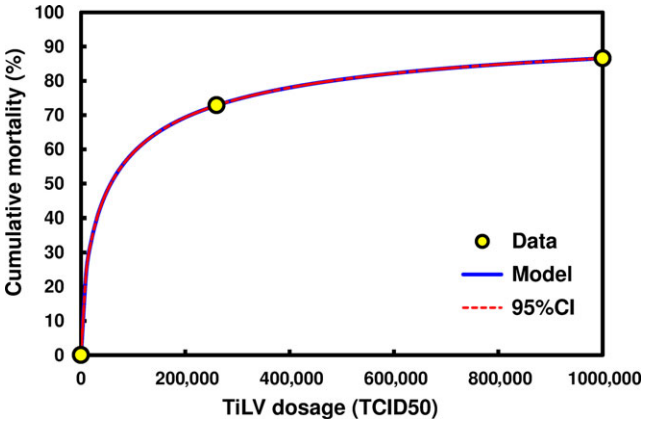

FIGURE 2 Reconstructed dose–response profile for relationship between TiLV doses and cumulative mortality of Nile tilapia posed by 1×10^6 and 2.6×10^5 TCID50 fish^{-1} TiLV via I.P. injection

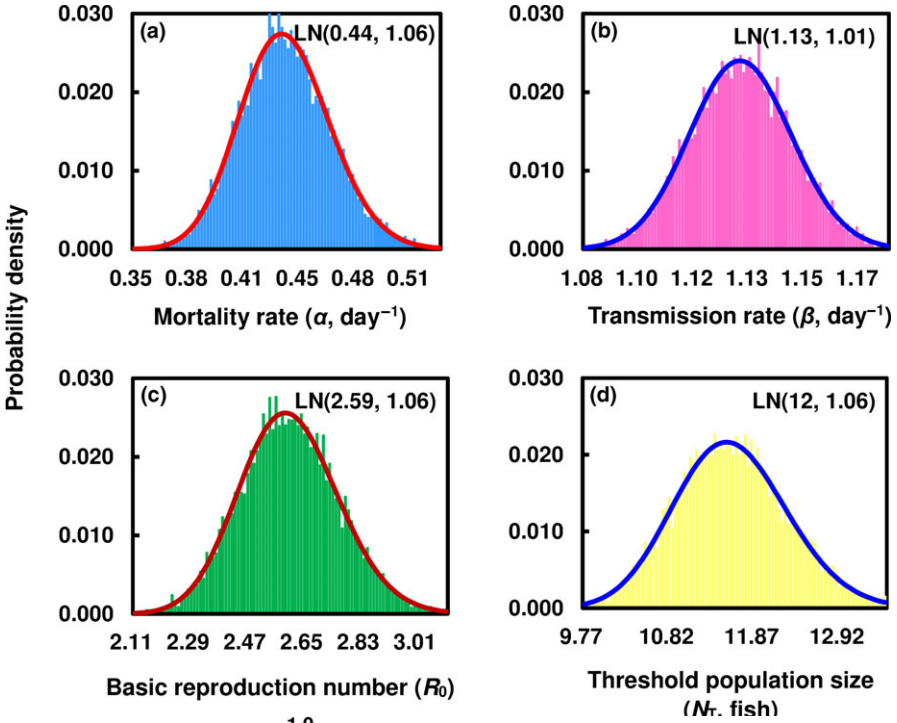

FIGURE 3 Probability distributions of (a) mortality rate (α), (b) transmission rate (β), (c) basic reproduction number (R_0) and (d) threshold population size (N_T) estimates of Nile tilapia posed by 2.6×10^5 TCID50 fish^{-1} TiLV under treatment of cohabitation

respectively (Figure 3a–c). For N_T estimation, the probability distribution of N_T was derived by multiplying N_T probability distribution in unit fractions (LN(0.39, 1.06)) with initial Nile tilapia size of 30, obtaining a GM and GSD of 12 and 1.06, respectively (Figure 3d).

3.3 | Population-associated dynamics of TiLV-infected tilapia via cohabitation

The SIM model that predicts cumulative mortality profiles significantly fitted the published cumulative mortality data of Nile tilapia posed by 2.6×10^5 TCID50 fish^{-1} TiLV via cohabitation, resulting in a root-mean-square error (RMSE) of 7.32% (Eyngor et al., 2014) (Figure 4a). Figure 4b illustrates probability distributions of force of infection (λ_F) of TiLV in Nile tilapia via cohabitation with estimates from 0.79 to 1.03. Moreover, our result shows an effective reduction in percentage of mortality for Nile tilapia posed by 2.6×10^5 TCID50 fish^{-1} TiLV via cohabitation (Figure 4c).

Results also revealed that population of Nile tilapia decreased to 12% of the initial population size after 16 days postinfection (Figure 4c). The highest number of infectious tilapia was found to be after 5 days post-TiLV infection (Figure 5). Moreover, fractions of tilapia in susceptible and mortality states were approximately 0.5 after 4–5 and 6–7 days, respectively, post-TiLV infections (Figure 5).

3.4 | TiLV disease control

Figure 6 illustrates the contour plot showing dependence of R_C on proportion of reductions in infection time (τ) and transmission rate (β). Results also show that the higher the proportion of reductions in infection time and transmission rate, the lower values of R_C

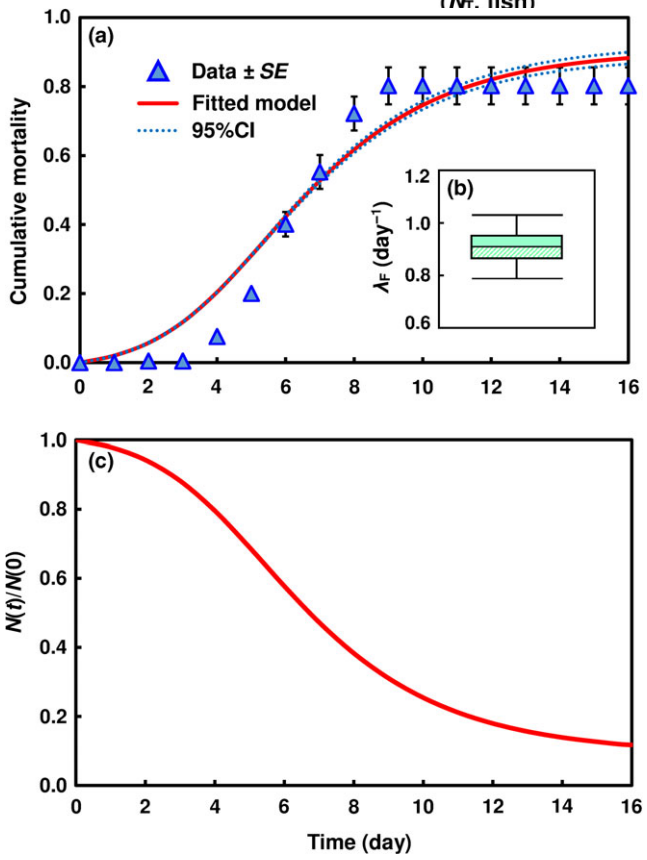

FIGURE 4 (a) Proposed population dynamics of disease model tested against the published cumulative mortality data of Nile tilapia posed by 2.6×10^5 TCID50 fish^{-1} TiLV under treatment of cohabitation. (b) Box and whisker plot of force of infection (λ_F, day^{-1}) estimate of Nile tilapia posed by 2.6×10^5 TCID50 fish^{-1} TiLV under treatment of cohabitation. (c) Simulated response curve of population dynamics of susceptible Nile tilapia subjected to 2.6×10^5 TCID50 fish^{-1} TiLV under treatment of cohabitation

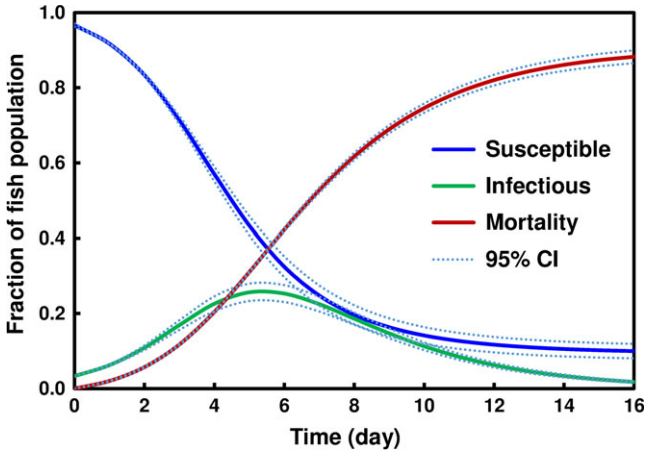

FIGURE 5 Simulation of population dynamics for Nile tilapia posed by 2.6×10^5 TCID50 fish^{-1} TiLV under treatment of cohabitation

(Figure 6a). Therefore, R_C can be restricted to be less than one if we implement appropriately the control strategies by controlling the effective contact rate and infection time (Figure 6a).

Moreover, the contour plot of threshold population or population size-dependent R_C control was demonstrated (Figure 6b). Results indicated that increments and decrements of proportion of reduction in N and N_T of hosts, respectively, could decrease values of R_C (Figure 6b). For example, outbreaks of TiLV disease could be contained ($R_C < 1$) when proportion of reduction in population size of tilapia was higher than 0.6 under a condition of less than 0.4 of proportion of reduction in threshold population size (Figure 6b).

3.5 | Sensitivity analysis

We performed a global sensitivity analysis on R_0 to determine quantitatively the most influential parameter on disease outbreak (Fig-

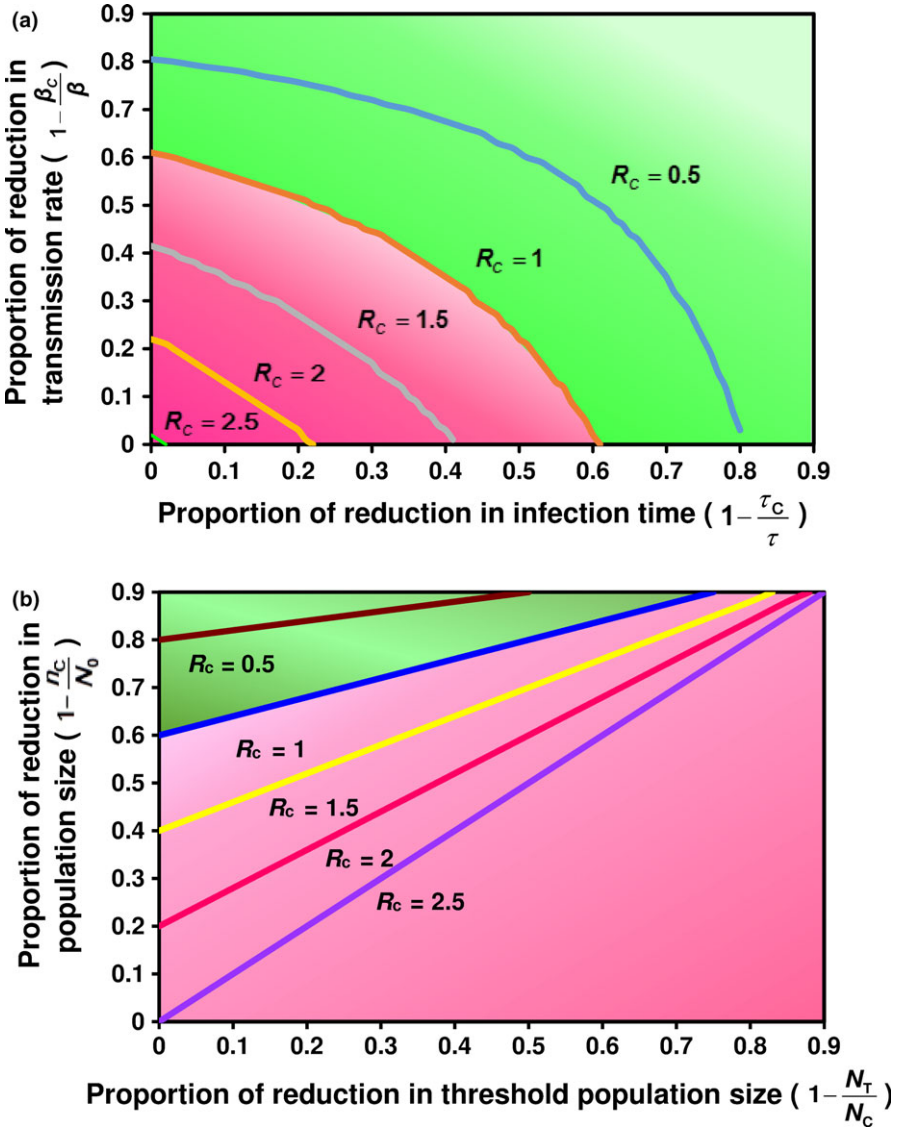

FIGURE 6 Contour plots of (a) proportion of reductions in infection time ($1 - \tau_C/\tau$)- and transmission rate ($1 - \beta_C/\beta$)-dependent and (b) proportion of reductions in threshold population size ($1 - N_T/N_C$)- and population size ($1 - n_C/N_0$)-dependent control lines of the control reproduction number R_C

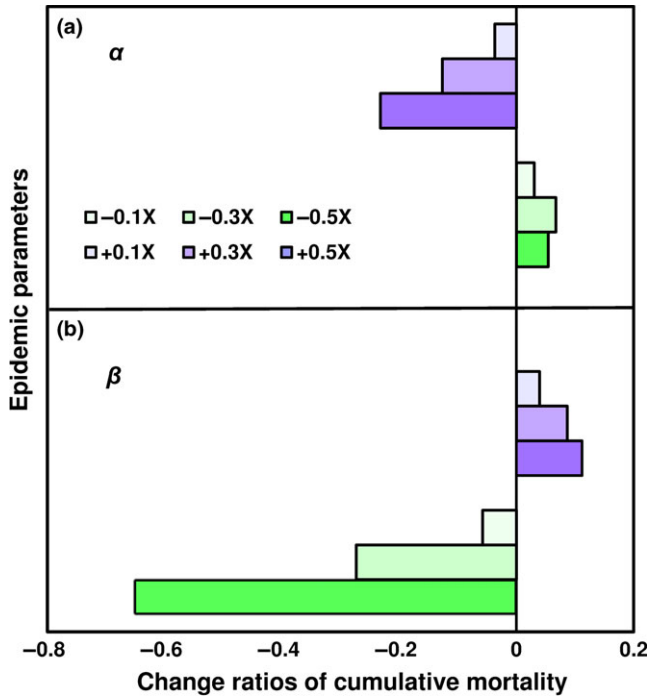

FIGURE 7 Sensitivity analysis for epidemic parameters of (a) mortality rate (α) and (b) transmission rate (β) against cumulative mortality change ratios of Nile tilapia subjected to TiLV infections

ure 7). Results indicate that ratios of cumulative mortality change negatively corresponding to increments and decrements of mortality and transmission rates, respectively (Figure 7). We also found that transmission rate was a more sensitive epidemic parameter to alternations of cumulative mortalities than mortality rate, implicating that transmission rate plays a critical role in controlling TiLV pandemics in aquaculture systems (Figure 7b).

4 | DISCUSSION

4.1 | Dynamics of TiLV transmission in cohabitation scenario

Although the TCID50 values were different in experimental settings of employed literature (Eyngor et al., 2014; Tattiyapong, Sirikanchana, & Surachetpong, 2018; Tattiyapong et al., 2017), Kembou Tsofack et al. (2016) demonstrated that values of TCID50 for E-11 cell line exposed to TiLV ranged from 1.6×10^5 to 4×10^6, consistent with applied doses of 2.6×10^5 and 1×10^6 TCID50 fish^{-1} in cohabitation and I.P. injection experiments, respectively (Eyngor et al., 2014; Tattiyapong et al., 2017). On the other hand, the optimal temperature for TiLV replications in both E-11 and primary tilapia brain cells was assessed to be 25°C, close to cohabitation scenario of Eyngor et al. (2014).

The transmission mode of TiLV was demonstrated to be through direct horizontal transmission instead of vertical transmission by cohabitation, indicating that TiLV infection is mainly transmitted through waterborne route (Eyngor et al., 2014). In particular, different to vertical transmission that is accompanied by intrinsic immune suppression of protective networks of progeny posed by maternally derived virus (Burnet, 1969; McCullagh, 1996; von Siebenthal, Jacob, & Wedekind, 2009), horizontal (or waterborne) transmission is an uncompromised fighting of virus in immune systems of healthy hosts. Therefore, upon infection with TiLV in tilapia, the virus is recognized as an exterior threat, generating immune responses in tilapia as a defensive mechanism to stressors.

4.2 | Effects of tilapia density on TiLV epidemics in aquacultural systems

Higher density of fish results in increased mortality rates, elevated viral loads and reduced body condition compared with fish in low density. In this study, we provided another perspective to contain outbreaks of TiLV disease with threshold population size (N_T) representing the initial number of susceptible hosts that require to initiate an epidemic. To prevent spreading of TiLV among tilapia population, the estimated threshold population size was 14 fish based on the study cohabitation setting of Eyngor et al. (2014). In aquaculture systems, confinement stress such as high densities of rearing fishes is more likely to weaken the immune systems, resulting in vulnerability to pathogen infections (Portz, Woodley, & Cech, 2006). Thrush, Murray, Brun, Wallace, and Peeler (2011) also revealed that high host density, poor environment and intercurrent disease (occurring during the course of another disease) undermined immunity in farmed stocks and reduced resistance to diseases while enhancing contact frequencies.

Moreover, Shoemaker, Evans, and Klesius (2000) reported that density had a significant effect on streptococcal disease mortality in tilapia exposed to *Streptococcus iniae* by immersion. Several studies also indicated that stocking density was inversely proportional to body weight, daily weight gain and length of Nile tilapia fingerlings that were closely associated with fish immunity (Breine, Nguenga, Teugels, & Ollevier, 1996; Gustafson, Ellis, & Bartlett, 2005; Inendino, Grant, Philipp, & Goldberg, 2005; Sanudi, Jere, Mzengereza, & Chirwa, 2015). Confinement stress was evidenced to suppress phagocyte-mediated reactive oxygen species (ROS) production, revealing that co-impact of virus and confinement stress to fish larvae without intact immune system could lead to lower tolerance and mass mortalities in farmed fish (Avtalion, 1981; Cubero & Molinero, 1997; Wise, Schwedler, & Otis, 1993).

4.3 | Aquaculture management strategies

As one of the most prominent food-producing industries, containment of fish disease outbreaks in aquaculture systems should be deeply concerned and solved. We simulated the population dynamics of Nile tilapia based on estimated transmission and mortality rates, providing useful information for aquaculture management to develop control measures at suitable time when TiLV disease occurs. It is an alternative approach for fisheries minimizing the loss under no drug treatment by population size reduction. Also, the well-simulated

disease progression is likely to assist the research and development of aquaculture drugs and vaccines to better control the endemic of epizootics.

Jansen and Mohan (2017) have recommended that biosecurity measures, intervention strategies such as vaccine developments as well as containment programmes should be improved to minimize the impact of TiLV in affected geographic regions. Therefore, containment tools and programmes of TiLV developed in the future can be incorporated with the model framework constructed in this study by integrating more compartmental systems (e.g., recovery population) when more intervention strategies are available. Moreover, Bondad-Reantaso, Subasinghe, and Arthur (2005) revealed that epidemiological research of TiLV disease should include risk and biological factors (e.g., at-risk population identifications, hazards, pathways, spread pattern, incubation period and nature of the pathogen), interventions and methodologies (e.g., surveillance techniques, disease outbreak modelling and use of geographic information systems) in future studies. On the other hand, whether the TiLV could be transmitted through frozen tilapia products or carried by nontilapine species and organisms such as piscivorous birds and mammals should also be deeply explored (FAO, 2017a).

Dong et al. (2017) reported that early stages of tilapia (fertilized eggs, fry and fingerlings) are most susceptible to TiLV infections. Surachetpong et al. (2017) also observed that significant mortalities of tilapia occurred during 1 month after transfer from hatchery to grow-out cages in public rivers or reservoirs (1-month mortality syndrome), implicating that biosecurity practices should be executed in early stages to prevent translocation of fry/fingerlings from TiLV-affected countries. It should also be noted that the contagiousness/transmission rate of TiLV could be various depending on culturing conditions and environmental parameters in local farmed ponds. In practical, to effectively prevent TiLV outbreaks in tilapia farmed ponds where uninfected tilapia are cohabitated with TiLV-infected ones, specific threshold population sizes should be rigorously estimated based on characteristics of local ponds by collecting in situ cumulative mortality data and applying the constructed model framework developed in this study.

Furthermore, Fathi et al. (2017) revealed that several management factors such as farm size and cocultivation contributed to TiLV-associated "summer mortality" syndrome of Nile tilapia. Moreover, farm size was a main contributor in transmission of infectious diseases among hydrodynamically linked farmed ponds, indicating that increments of separation distance between farmed ponds significantly prevent pathogen transmission (Salama & Murray, 2011). Kabuusu, Aire, Stroup, and Ferguson (2018) also suggested that controlling number of pond production cycles per year and elevating weight of fish at time of transfer during culture seasons could also be practical approaches for aquaculture management. Taken together, to rigorously reinforce TiLV containment, control of fish density by employing the developed model framework can be accompanied with other administrative strategies of managing farm size and production cycles, and limiting cocultivation in tilapia farms in different geographic areas.

4.4 | Limitations and implications

Compared to pathogens of bacteria or protozoa, there are relatively limited numbers of virus family that have been reported as aetiological agents of tilapia diseases. Several studies indicated that the lymphocystis and Bohle virus and infectious pancreatic necrosis, belonging to the family of iridovirus and Birnaviridae, respectively, were pathogenic for tilapia species (Ariel & Owens, 1997; Hedrick, Fryer, Chen, & Kou, 1983; Mangunwiryo & Agius, 1987; Paperna, 1973). In addition, viral encephalopathy and retinopathy, categorized as nodavirus, are more likely to cause high mortality rates in larval stages, resulting in economic losses in aquaculture tilapia. Therefore, exploration of disease transmission dynamics of waterborne pathogens is paramount and crucial for sustainability of economically valuable fisheries.

To control outbreaks of fish diseases, Snieszko (1958) suggested that an artificial balance should be established by selection and breeding of disease-resistant fish species. Ferguson et al. (2014) indicated that pathogenicity of TiLV was various among different tilapia species in that one strain called genetically all male (GMT–also *O. niloticus*) incurred significantly lower mortality (10%–20%) compared to other tilapia strains, indicating that GMT cultivation could be considered as an intervention strategy for prevention of TiLV disease outbreaks. On the other hand, lower replications of TiLV RNA levels were observed at culture conditions of higher (30°C) and lower (20°C) temperatures, implicating that manipulation of optimal aquaculture temperatures could be treated as an efficient strategy for TiLV disease containments (Kembou Tsofack et al., 2016).

The distinct role of disease transmission in aquatic animal population dynamics has received little concerns (Longshaw, Frear, Nunn, Cowx, & Feist, 2010). Although most epidemiological models reviewing the interaction between disease and host dynamics exist for terrestrial populations (Anderson & May, 1979), the principles governing spread of diseases of humans and other mammals should be applicable to infectious diseases in fish with modification (Reno, 1998). The application of basic principles from epidemiological modelling to aquatic ecosystems has been reported by Reno (1998), in which the approach has been successfully adopted to predict the spread of disease between fish farms (Jonkers, Sharkey, Thrush, Turnbull, & Morgan, 2010; Taylor, Norman, Way, & Peeler, 2010). A recent study also estimated transmission dynamics of proliferative kidney disease in salmonid populations with application of epidemiological model (Carraro et al., 2016).

In particular, the SIM model constructed in this study is a deterministic and compartmental model to analyse dynamic interactions between virus and host populations. Furthermore, the methodology and modelling framework developed can mechanistically estimate transmission dynamics of TiLV among tilapia population in various culture conditions with different water volume and fish numbers. On the other hand, due in part to the limited information of cumulative mortality data of TiLV-infected tilapia in cohabitation or other culturing conditions, we aim to validate, modify and refine the constructed model by integrating the most important factors when more results

of infection experiments are available. Also, our disease model structure can be generalized to other aquaculture diseases and strengthen dynamic simulation with collected data and estimated parameters.

On the other hand, Amal et al. (2018) found that synergistic co-infection of TiLV with other pathogens aggravated threats to global tilapia industry. Nicholson et al. (2017) also indicated that bacterial infection of *Aeromonas* species was related to the high summer mortalities in Egyptian fish farms, implicating that co-infections of pathogenic *Aeromonas* species along with TiLV should be further explored. Moreover, the various transmission dynamics among the divergent form of the Egyptian TiLV strain and the Ecuadorian and Israel strains should be compared and characterized (Nicholson et al., 2017).

In conclusion, with respect to the rapid dissemination of TiLV in tilapia farmed ponds among multi-continents, our results provide insights into implementation of biosecurity enforcement, effective control measures and intervention strategies such as vaccine and diagnostic developments. We also provide information regarding population dynamics, epidemiological parameters and tactical management strategies based on mathematical modelling for future TiLV infection. Furthermore, our findings provide aquaculture engineers and public health scientists the unparalleled mechanistic assessment to reduce waterborne diseases in aquaculture farming systems. Most importantly, international collaborative programmes of tilapia ponds in private sectors and related government agencies may facilitate to promote management practices in defence of further impacts and spreading of the emerging viral disease in global aquaculture systems.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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