Genetic parameters for resistance to Tilapia Lake Virus (TiLV) in Nile tilapia (Oreochromis niloticus)

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Abstract
Tilapia Lake Virus (TiLV) is one of the primary disease concerns for tilapia farming, with mass mortality events and biosecurity restrictions threatening aquaculture in several continents. Selective breeding for improved host resistance to TiLV may help to mitigate this problematic disease, but the extent of genetic variation in resistance is not yet known. The objective of the current study was to estimate genetic parameters for host resistance to TiLV in a Nile tilapia breeding population of the Genetically Improved Farmed Tilapia (GIFT) strain. Using data from 1821 pedigreed fish (from 124 full-sibling families) collected during and after a pond ‘field’ outbreak, resistance was defined using both binary survival (BS) and days to death (TD) traits. Animal and sire-dam linear models were fitted for BS and TD, and BS was also evaluated with using two sire-dam threshold models with either probit (Pro-SD) or logit-link (Log-SD) functions. Cumulative mortality was 39.6% at the end of the outbreak, with family survival rates ranging from 0 to 100%. Moderate to high heritability values were estimated for resistance to TiLV using all models. Significant heritabilities were estimated on the binary scale (0.40 for both animal and sire-dam models) which equates to 0.63 on the underlying liability scale. Using threshold models, heritabilities of 0.56 and 0.48 were estimated for Pro-SD and Log-SD, respectively. Correlation among the full-sib families EBVs predicted by the different models ranged from 0.912 to 0.999, suggesting a low re-ranking of the families and a high consistency of the results obtained using the different models. In addition, significant and moderate heritability of 0.41 (0.06) was estimated for harvest weight (HW), and the genetic correlation between this trait and resistance to TiLV was not statistically different from zero. These results demonstrate that host resistance to TiLV is highly heritable in a Nile tilapia breeding population with GIFT origin. Therefore, selective breeding to increase resistance and reduce mortalities due to TiLV is a feasible and promising approach.

1. Introduction

Nile tilapia (Oreochromis niloticus) is among the most important aquaculture species farmed worldwide. According to the Food and Agriculture Organization of the United States (FAO), the production of tilapia reached approximately 6.2 million tons during 2016, representing one of the major sources of animal protein for human consumption (FAO, 2018), particularly in developing countries in Asia, South America, and Africa (Shelton and Popma, 2006).

However, as with other intensive production systems, infectious disease is one of the main issues threatening the success and sustainability of tilapia production. A relatively new pathogen, the orthomyxovirus-like Tilapia Lake Virus (TiLV) has emerged as a major threat for Nile tilapia (Eyngor et al., 2014; Fathi et al., 2017; Mugimba et al., 2018; Pulido et al., 2019), and also for other farmed tilapias, including red tilapia (Oreochromis sp.) and hybrid strains (O. niloticus × O. aureus) (Eyngor et al., 2014; Surachetpong et al., 2017). Although the virus was discovered in 2014, it may have been responsible for mortalities since 2008–2009 (Bacharach et al., 2016; Eyngor et al., 2014). To date, it has been identified in countries from different geographical regions and continents, including Peru (Pulido et al., 2019), Ecuador (Bacharach et al., 2016), Malaysia (Amal et al., 2018), India (Behera et al., 2018), Thailand (Dong et al., 2017), Egypt (Fathi et al., 2017) and Uganda (Mugimba et al., 2018).

The agent is a novel single-stranded orthomyxo-like RNA enveloped virus, with a diameter ranging from 55 to 100 nm (Bacharach et al., 2016, 2018). It is capable of causing mass mortalities in tilapia farms, with family survival rates varying from 0 to 100%. The disease is mediated by a single-stranded RNA genome and is highly contagious, rapidly spreading through the affected populations.

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2016; Del-Pozo et al., 2017; Eyngor et al., 2014). The virus can cause disease in several stages of the tilapia life-cycle, from fingerlings to adults (Ferguson et al., 2014; Senapin et al., 2018), and in multiple organs such as spleen, heart and brain, and even in the reproductive organs, and can be transmitted vertically (Dong et al., 2020). However, some studies suggest a higher prevalence of the virus in kidney, gills and liver (Bacharach et al., 2016; Dong et al., 2017; Mugimba et al., 2018). The clinical signs may vary depending on the geographical origin, and include skin erosion and darkening, gill pallor, anemia and swollen abdomen (Dong et al., 2017; Ferguson et al., 2014), with subclinical infections also being reported (Senapin et al., 2018).

Tilapia Lake Virus (TLV) can cause high levels of mortalities, but these can vary substantially (ranging from 5 to 90%) in disease outbreaks, which are usually observed within the subsequent weeks post-transfer from hatcheries to growth out ponds (Dong et al., 2017; Fathi et al., 2017). After these outbreaks, it has been shown that surviving fish have a higher resistance to this infection to subsequent outbreaks suggesting some degree of resistance via acquired immunity (Eyngor et al., 2014). For a detailed review about TLV diagnosis, mitigation and control measurements, please see Jansen et al. (2018).

Selective breeding for genetic improvement of tilapia is increasingly used to improve production traits. To date, tilapia breeding programs have included growth-related traits as an objective of selection, reaching genetic gains ranging between 10 and 15% per generation (Ponzoni et al., 2011), highlighting the feasibility of improving production traits by means of selective breeding (Gjedrem and Rye, 2018). In case of infectious diseases, selective breeding is a sustainable strategy to reduce the mortality rate, enhance disease resistance and increase welfare and productivity (Stear et al., 2001).

One approach to improve disease resistance is based on controlled challenge tests. This methodology allows for control of environmental variables and evaluation of one specific pathogen at a time. Generally, the trait of resistance is assessed by infecting the host by cohabitation, immersion or intraperitoneal injection, and ideally selecting a pathogen strain identical to the observed in the field (Houston, 2017; Ødegård et al., 2011a; Yáñez et al., 2014). A second alternative, is to collect samples and data from outbreaks of disease in production environments (i.e. field outbreak). While the latter is potentially the most relevant source of data to quantify genetic resistance, it is often difficult to obtain high quality samples and confirm the cause of death. However, both approaches have their own advantages and drawbacks, and both can be successfully used to improve disease resistance, and a high genetic correlation between disease resistance traits measured using the two methods has previously been shown for some diseases (Gjøen et al., 1997; Ødegård et al., 2006). A wide range of studies have showed the viability of improving disease resistance to specific pathogens via selective breeding in a variety of aquaculture species, including European sea bass (Dicentrarchus labrax) (Palaiokostas et al., 2018), Pacific oyster (Crassostrea gigas) (Gutierrez et al., 2018a), Pacific white shrimp (Penaeus vannamei) (Ødegård et al., 2011b), and in the three main farmed salmonids species i.e. Atlantic salmon (Salmo salar), (Correa et al., 2015) rainbow trout (Oncorhynchus mykiss) (Vallejo et al., 2017) and coho salmon (Oncorhynchus kisutch) (Barria et al., 2019). For a reviews of genetic improvement of disease resistance in aquaculture species, please see Houston (2017) and Yanez et al. (2014).

In case of tilapia, several studies have estimated significant genetic variation for resistance to bacterial pathogens in controlled challenge experiments (LaFrentz et al., 2016; Shoemaker et al., 2017; Wonmongkol et al., 2018). However, despite the serious consequences of TLV-related infections, there are no published estimates of quantitative genetic parameters for resistance to TLV, and its potential to be improved by selective breeding, and this is likely to be due to the current lack of a well-established and effective TLV challenge model, although these have begun to be established (Jaemwimol et al., 2018; Pierzean et al., 2019; Tattiyapong et al., 2017).

Therefore, the aim of the current study was to estimate the levels of genetic variation for resistance to Tilapia Lake Virus in a population of Nile tilapia from the GIFT strain, using data collected from a field outbreak of the disease. In addition to estimating heritability values under different statistical models, the genetic correlation with harvest weight was also assessed. The results will inform improvement of this trait by means of selective breeding to help develop more resistant tilapia strains which can help mitigate and potentially control this problematic disease.

2. Materials and method

2.1. Study population

The Nile tilapia population used in the current study was from a major breeding program established in Malaysia and managed by WorldFish. This population originated from the GIFT strain, and has been selected for improved growth rate for 15 generations. A total of 124 families were produced using 115 sires and 124 dams. To retain pedigree information, each individual was tagged with a Passive Integrated Transponder (PIT) tag at an average weight and age of 4.97 g and 110.5 days, respectively. Once individuals reached typical harvest weight, their weight was recorded and they were transferred to a single pond, after which a Tilapia Lake Virus outbreak was observed.

2.2. Tilapia Lake Virus outbreak

This population experienced a natural TLV outbreak in February 2018. Survival or mortality data were obtained from a total of 1821 fish from a single pond, and this formed the basis of the trait of TLV resistance. An average of 14 fish (ranging from 2 to 21) per family were measured for TLV resistance. Fish were collected until the mortality curve had stabilized, i.e. mortalities had returned to baseline levels. Sex was identified for all fish, with a male:female ratio of 0.74:1.00. Surviving fish were euthanized with clove oil (400 mg/l). Necropsy assays were performed on a number of randomly selected dead fish to evaluate the cause of death and corroborate with the observed clinical signs of the disease. To confirm the presence of TLV, spleen samples were obtained from a random sample of 39 individuals. The spleen tissue was maintained in RNALater and kept at -20 °C until analysis.

2.3. Trait definitions

Resistance to TLV was defined as binary survival (BS) and time to death (TD). For the former, survivors and dead fish were assigned values of 1 and 0, respectively. In case of TD the values ranged from 1 (first day of observed mortalities) to the last collection day (19). Survivor fish were assumed as censored data and each assigned the value of 18 or 19 days based on the sampling day.

2.4. Statistical analyses

Linear and threshold models were fitted to estimate heritabilities of the measured traits, using a restricted maximum likelihood method. Only significant fixed effects (p < .05) were included in the final models used for each trait, and this was assessed using Wald F statistics.

Six different models were fitted for resistance to TLV as follows, using the ASREML software (Gilmour et al., 2009) v.4.1:

Model 1: Binary survival, animal linear model (BS-LAN):

\[ Y_{ij} = \mu + SEX_i + b_1 HW_i + b_2 HA_i + a_i + e_{ij} \]

Binary survival data was assessed using a linear mixed model, where \( Y_{ij} \) is the binary survival outcome (1 = survivor, 0 = dead) of fish \( i \), \( \mu \) is the overall mean, \( SEX \) is the effect of fish gender on survival, \( HW \), and \( HA \) are the covariates harvest weight and harvest age of the fish, respectively, \( a_i \) is the random additive genetic effect of animal \( i \), \( e_{ij} \) is the random residual effect, and \( b_1 \) and \( b_2 \) are the regression coefficients of...
harvest weight and harvest age, respectively.

Model 2: Time to death, animal linear model (TD-LAN):

\[ Y_{ij} = \mu + SEX_i + \beta_1 HW_i + \beta_2 HA_i + a_i + e_{ij} \]

where \( Y_{ij} \) is the time to death of fish \( i \), varying from 1 to 19. The other parameters are as described above.

Model 3: Binary survival sire-dam probit link model (Pro-SD):

The followig probit link function was assessed

\[ \Pr(Y_{iak} = 1) = \frac{1}{1 + \exp(-\mu + SEX_i + \beta_1 HW_i + \beta_2 HA_i + S_j + D_k + \epsilon_{iak})} \]

where \( Y_{iak} \) is the binary survival outcome (1 = survivor, 0 = dead) of fish \( i \). \( S_j \) is the random additive genetic effect of sire \( j \), \( D_k \) is the random additive genetic effect of dam \( k \), \( \epsilon_{iak} \) is the random residual effect, and \( \phi () \) is the standard normal cumulative distribution function. The other parameters are as described above.

Model 4: Binary survival sire-dam logit link model (Log-SD):

The following logit link function was assessed

\[ \Pr(Y_{iak} = 1) = \frac{1}{1 + \exp(-\mu + SEX_i + \beta_1 HW_i + \beta_2 HA_i + S_j + D_k + \epsilon_{iak})} \]

where \( Y_{iak} \) is the binary survival outcome (1 = survivor, 0 = dead) of fish \( i \). The other parameters are as described above.

Model 5: Binary survival, sire-dam linear model (BS-SD):

\[ Y_{ijk} = \mu + SEX_i + \beta_1 HW_i + \beta_2 HA_i + S_j + D_k + \epsilon_{ijk} \]

where \( Y_{ijk} \) is the binary survival outcome (1 = survivor, 0 = dead) of fish \( i \). The other parameters are as described above.

Model 6: Time to death, sire-dam linear model (TD-SD):

\[ Y_{ijk} = \mu + SEX_i + \beta_1 HW_i + \beta_2 HA_i + S_j + D_k + \epsilon_{ijk} \]

Where \( Y_{ijk} \) is the time to death of fish \( i \). The other parameters are as described previously.

For the trait of harvest weight (HW), the following univariate linear animal model was assessed:

\[ Y_{ij} = \mu + SEX_i + \beta_1 WT_i + \beta_2 HL_i + \beta_3 HA_i + a_i + e_{ij} \]

where \( Y_{ij} \) is the HW of fish \( i \), \( \mu \) is the overall mean, \( SEX_i \) is the effect of the fish gender on harvest weight, \( WT_i \), \( HL_i \), and \( HA_i \) are the covariates weight at tagging, harvest length, and harvest age of the fish, respectively, \( a_i \) is random additive genetic effect of animal \( i \), \( e_{ij} \) is the random residual effect, and \( \beta_1, \beta_2 \) and \( \beta_3 \) are the regression coefficients of WT, HL and HA, respectively.

Finally, a bivariate linear animal model was assessed to estimate the (co)variance between HW and both resistance traits (BS and TD). Due to the fact that HW is included as a response variable in both bivariate models, it was not included as an explanatory variable for TD or BS.

### 2.5. Heritability and genetic correlations

For model 1 and 2, heritability was estimated as follows:

\[ h^2 = \frac{\sigma^2_A}{\sigma^2_G + \sigma^2_e} \]

where \( \sigma^2_A \) is the genetic additive variance, and \( \sigma^2_e \) is the residual variance. This formula was also used for HW.

For the sire-dam models, the sire and the dam variance were assumed to be equal. i.e. \( \sigma^2_A = \sigma^2_s = \sigma^2_d \) with variance \( \sim \mathcal{N}(0, A\sigma^2) \), where \( A \) is the additive genetic relationship matrix among individuals. Residual variance was assumed as \( \sim \mathcal{N}(0, I\sigma^2_e) \).

As the sire-dam variance is expected to correspond to ¼ of the total genetic additive variance, heritability estimation for models 3-6 were as follows:

\[ h^2 = \frac{4\sigma^2_A}{2\sigma^2_A + \sigma^2_e} \]

where \( \sigma^2_A \) is the sire-dam additive genetic variance, and \( \sigma^2_e \) is the residual variance.

In case of Pro-SD and Log-SD, the residual variance used to estimate \( h^2 \) was 1 and \( \pi^2/3 \), respectively (Gilmour et al., 2009).

For BS-LAN and BS-SD the estimated heritability on the observed binary scales were converted to the underlying liability scale by the following formula proposed by Dempster and Lerner (1950)

\[ h^2 = h_0^2 \cdot \frac{1-p}{p} \]

where \( h_0^2 \) is the heritability estimated for the observed binary scale, \( p \) is the proportion of dead individuals in the population and \( i \) is the mean deviation (in standard deviation units) of dead individuals from the population mean.

The genetic correlations \( (r_{xy}) \) among traits were calculated according to Falconer and Mackay (1996):

\[ r_{xy} = \frac{\sigma_{xy}}{\sqrt{\sigma^2_{xx} \sigma^2_{yy}}} \]

where, \( \sigma_{xy} \) is the additive genetic covariance between \( x \) and \( y \), \( \sigma^2_{xx} \) corresponds to the additive genetic variance of \( x \) and \( \sigma^2_{yy} \) corresponds to the additive genetic variance of \( y \).

### 2.6. Model comparisons

A Pearson and Spearman correlation analysis was performed among the full-sib family EBVs predicted by each model, as a measure of the consistency of the parameter estimates obtained using the different statistical models. Furthermore, due to the fact that the tested models used different trait definitions, these were compared based on their accuracy of selection, i.e. the correlation of the estimated breeding value (EBV) among full-sib families. Thus, outbreak data were randomly partitioned into two subsets (dataA = 911 fish and dataB = 910 fish), and the estimated variance components used were those estimated previously using the complete data set. The accuracy of selection (\( r_s \)) prediction was estimated as the square root of the Pearson correlation between full-sib families EBVs (\( r_{EBV} \)) predicted by each data subset (Gitterle et al., 2006; Yáñez et al., 2013). In the case of the animal models, the EBV for each full-sib family was predicted as the average EBV value of the parents, whereas for the sire-dam models, EBVs were predicted as \( Sire_{EBV} + Dam_{EBV} \).

### 3. Results

#### 3.1. TiLV mortalities

Throughout the TiLV outbreak, clinical signs typical of TiLV infection were observed by a qualified veterinary expert. These included skin erosion, hemorrhage, and damage on the base of the pectoral and anal fin. The presence of TiLV was confirmed in 73.5% of the analyzed samples (\( n = 25 \)). All 16 mortalities tested were positive for TiLV, while 9 survivors were positive and 9 survivors were negative for the virus. An average mortality rate of 56 fish per day was observed during the first five days of mortalities due to the outbreak. This mortality rate had a peak of 128 dead fish at day 10 after the first mortality was collected (Fig. 1S). After this, mortality rate declined to seven fish per day for four days later. During the last two days of data and sample collection (18th and 19th after the first mortality was registered) no mortalities were observed (Fig. 2S). The total cumulative mortality in the entire naturally exposed population (\( n = 1821 \)) at the end of the TiLV outbreak was 39.6%. Furthermore, following assignment of mortalities and survivors to family using the PIT tags, a high between-family variation in mortality level was observed, ranging from 0 to 100%. (Fig. 1), suggestive of additive genetic variation in resistance. A cox proportional hazard model estimates no significant difference in mortality rate
between sexes ($p = .529$).

3.2. Phenotypic variation

At tagging, fish had an average weight of 4.97 g, with a minimum and maximum weight of 1.20 and 19.0 g, respectively (Table 1). Fish were transferred to the facilities where the TiLV outbreak was observed at an average weight of 280.5 g, ranging from 129.2 to 467.8 g, while the mean length was 19.1 (SD = 1.23) cm. At the time of transfer, the age of fish varied from 188 to 263 days, with an average of 216.4 days. The time to death ranged from day 1 to 17, with an average of 9.97 days. Therefore, the TD distribution was right skewed with only 720 animals (39.6%; i.e. the mortalities) having a value ≤ 17, with the remainder being survivors, which were assigned a value of 18 or 19, based on the sampling day. The distribution of frequencies for the traits of HW, HA, BS and TD is shown in Fig. 3S.

3.3. Estimated heritabilities and genetic correlation

Significant additive genetic variation was estimated along the different models for both resistance traits in the current Nile tilapia population (Table 2). The estimated heritability values on the observed binary scale were identical between animal and sire-dam models (0.40 ± 0.06). Once converted to the underlying liability scale, this value equates to an estimated heritability of 0.63. The Pro-SD and Log-SD models resulted in similar estimated heritabilities of 0.56 (0.08) and 0.48 (0.07), respectively. For resistance defined as TD, heritability was 0.23 (0.05) and 0.24 (0.05) for TD-LAN and TD-SD model, respectively.

Table 2

| Model   | Method               | Heritability (± s.e.) |
|---------|----------------------|-----------------------|
| BS-LAN  | Observed binary scale| 0.40 (0.06)           |
|         | Underlying liability scale | 0.63                   |
| TD-LAN  | Time to death         | 0.23 (0.05)           |
| Pro-SD  | Probit-link scale     | 0.56 (0.08)           |
| Log-SD  | Logit-link scale      | 0.48 (0.07)           |
| BS-SD   | Observed binary scale | 0.40 (0.06)           |
|         | Underlying liability scale | 0.63                   |
| TD-SD   | Time to death         | 0.24 (0.05)           |

1 The used models were: BS-LAN = Binary survival animal linear model; TD-LAN = Animal linear model; Pro-SD = Sire-dam probit model; Log-SD = Sire-dam logit model; BS-SD = Binary survival sire-dam linear model; TD-SD = Sire-dam linear model.

value for harvest weight (0.41 ± 0.06, Table 3). In addition, there was no evidence of a genetic correlation between HW and resistance to TiLV measured as BS ($−0.10 ± 0.13$) or TD ($−0.05 ± 0.14$). No significant common environmental effect was detected for either TiLV resistance or harvest weight.

3.4. Model comparisons

Pearson and spearman correlation coefficients among the full-sib Table 3

| Trait | $r_s$    | $r_p$    | $h^2$   |
|-------|----------|----------|---------|
| BS    | $−0.10\pm(0.13)$ | $−0.04\pm(0.03)$ | $-$     |
| TD    | $−0.05\pm(0.14)$ | $−0.03\pm(0.03)$ | $-$     |
| HW    | $-$      | $-$      | $0.41\pm(0.06)$ |
families EBVs predicted by the six different models are shown in Table 4. These correlations ranged from 0.912 to 0.999, with the spearman approach resulting in slightly higher values. For both analyses, a lower correlation value was estimated when comparing BS-LAN and TD-SD with value of 0.912 and 0.928 for Pearson and spearman correlation, respectively. Whereas the higher correlations were found for BS when sire-dam models were used, with values ranging from 0.997 to 0.999. This consistency demonstrates that the statistical model used has little impact on the estimation of the breeding values for host resistance to TiLV.

In general, all the models show a high prediction accuracy as assessed by the correlation between full-sib EBVs in the data subsets, with values ranging from 0.796 to 0.860 (Table 5). For TD and BS, both animal and sire-dam models led to almost identical estimation. The lower accuracies were predicted when a linear model for TD was assessed independently if an animal (TD-LAN) or sire-dam (TD-SD) model was used (0.796 and 0.815, respectively).

### 4. Discussion

Tilapia Lake Virus (TiLV) has been a significant source of morbidity and mortality in various farmed Nile tilapia populations around the world, and is a currently major barrier to sustainable and profitable tilapia aquaculture. In the current study, host resistance to TiLV was found to be significant and high in a Nile tilapia breeding population with GIFT origin, using data collected during a field outbreak. These results highlight the significant potential of harnessing selective breeding to improve host resistance to TiLV in farmed Nile tilapia populations.

The current study utilized a natural ‘field’ disease outbreak to assess genetic resistance to TiLV. Typically, data for the genetic improvement of disease resistance traits are derived from controlled experimental challenges (Ødegård et al., 2011a; Yáñez et al., 2014), which allows control of environmental factors. However, the use of survival data from natural field outbreaks can be a feasible alternative in genetic programs for aquaculture species (Bangera et al., 2014; Dégremont et al., 2015; Houston et al., 2008; Lillehammer et al., 2013). There are advantages to using such field data, because it reflects the natural method of infection of the agent in terms of time of exposure and its spread within the population. For example, in contrast to experimental injection of fish with a pathogen, a field challenge also requires that the pathogen surpasses the host barrier function, and this may be an important component of host genetic variation. However, obtaining high quality data and samples from a field outbreak is challenging, in part due to the difficulty to be sure that mortality is due to the pathogen under study. With this in mind, the outbreak of TiLV in the fish used in the current study was first analyzed by an expert veterinarian examining clinical signs Secondly, necropsy assays on the lesions observed on the fish attributed to this viral infection process, strongly suggest that TiLV was the major reason for the mortalities. Finally, the presence of TiLV in all of the tested mortalities and a proportion of survivors was confirmed by qPCR. The reasons for the absence of TiLV in some of the survivors could be due to the fish being resistant to the virus, and therefore potentially able to remove or reduce viral particles to a level below the detection threshold of the assay.

The detection of significant additive genetic variation for resistance to TiLV and the estimation of high heritability values is consistent with findings from other important infectious diseases in aquaculture species (e.g. Gonen et al., 2015; Kjøglum et al., 2008; Ødegård et al., 2006; Rodriguez et al., 2019; Shoemaker et al., 2017). Furthermore, the higher heritability estimated with threshold models than with linear models are in accordance with previous findings (e.g. Shoemaker et al., 2017; Sukhavachana et al., 2019; Yáñez et al., 2013) as are the high genetic correlation (0.95) between both resistance trait definitions (e.g. Barria et al., 2019; Bassini et al., 2019) highlighting that both binary survival and days to death are genetically the same trait using the methodology of the current study. This is to be expected to some extent since the majority of fish were survivors, and they were assigned a single value (1) for binary survival, and one of two values (18 or 19) for days to death.

Differences in the analysis and the definition of resistance can impact on the heritability estimates and their interpretations. Despite the fact that the cumulative mortality throughout the TiLV outbreak was below 50%, at which the phenotypic variance for a binary trait is maximized, significant heritability was estimated using both probit and logit-link functions. As shown in other studies into genetics of disease resistance in aquaculture species (Bangera et al., 2014; Ødegård et al., 2007, 2006; Yáñez et al., 2013), a high correlation among family ranking was estimated using the different models, revealing a low re-ranking of the families genetically more resistant to TiLV. Furthermore, and although heritabilities for BS-SD were slightly lower than the threshold models, selection accuracy remained high and similar breeding values were predicted among these approaches. In case of resistance measured as time to death, an identical heritability estimation and correlation between full-sib families’ EBVs was found between TD-LAN and TD-SD. These results suggest that binary survival is an appropriate measure of resistance to TiLV and time to death does not add additional useful information in this context.

Although high selection accuracy was estimated for TiLV resistance, selection of individuals based on the pedigree data is less accurate than when genomic data is available, as has been demonstrated on other farmed aquaculture species for growth-related traits (e.g. Gutierrez et al., 2018b; Tsai et al., 2015) and for disease resistance (e.g. Bangera et al., 2017; Barria et al., 2018; Correa et al., 2017; Ødegård et al., 2014; Tsai et al., 2016; Yoshida et al., 2018b; Yoshida et al., 2018a) by means of genomic selection (GS). Recently, high-density SNP arrays have been developed for different Nile tilapia (Joshi et al. 2018a; Yáñez et al., 2020; Penaloza et al. in prep) populations with GIFT origin. The use of these technologies will most likely help to increase the selection

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### Table 4

| Model       | BS-LAN | TD-LAN | Pro-SD | Log-SD | BS-SD | TD-SD |
|-------------|--------|--------|--------|--------|-------|-------|
| BS-LAN      | 1      | 0.918  | 0.994  | 0.994  | 0.998 | 0.912 |
| TD-LAN      | 0.934  | 1      | 0.926  | 0.926  | 0.922 | 0.998 |
| Pro-SD      | 0.995  | 0.938  | 0.998  | 0.997  | 0.925 |       |
| Log-SD      | 0.995  | 0.938  | 0.999  | 1      | 0.997 | 0.925 |
| BS-SD       | 0.996  | 0.937  | 0.999  | 1      | 0.999 | 0.919 |
| TD-SD       | 0.928  | 0.997  | 0.937  | 0.938  | 0.934 | 1     |

1. The models used were: BS-LAN = Binary survival animal linear model; TD-LAN = Animal linear model; Pro-SD = Sire-dam probit model; Log-SD = Sire-dam logit model; BS-SD = Binary survival sire-dam linear model; TD-SD = Sire-dam linear model.

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### Table 5

| Model       | \(r_{ABV}\) | \(r_a\) |
|-------------|-------------|--------|
| BS-LAN      | 0.718       | 0.847  |
| TD-LAN      | 0.635       | 0.796  |
| Pro-SD      | 0.729       | 0.854  |
| Log-SD      | 0.737       | 0.859  |
| BS-SD       | 0.740       | 0.860  |
| TD-SD       | 0.664       | 0.815  |

1. The models used were: BS-LAN = Binary survival animal linear model; TD-LAN = Animal linear model; Pro-SD = Sire-dam probit model; Log-SD = Sire-dam logit model; BS-SD = Binary survival sire-dam linear model; TD-SD = Sire-dam linear model.
response for this disease in the current breeding population by increasing the accuracy of selection and therefore reduce the mortalities ascribed to TiLV, as has been recently shown for responses to growth and fillet yield in Nile tilapia (Yoshida et al., 2019). Furthermore, the genotype data obtained from these SNP arrays will allow investigation of the genetic architecture of TiLV resistance, and whether there are significant QTL contributing to the genetic variation in the trait.

Moderate and significant genetic variation was also identified for harvest weight in the current study, which is in agreement with previous results in tilapia populations (Bentsen et al., 2012; Joshi et al., 2018b; Khaw et al., 2016; Marjanovic et al., 2016). Previous studies have shown different results in terms of genetic correlation between growth-related traits and disease resistance. The genetic correlations vary from negative (Yáñez et al., 2016), not different from zero (Silverstein et al., 2009) to positively correlated (Barria et al., 2019), depending on the age of the fish and the growth trait under study (i.e. body length, early growth rate, weight at harvest). The fact that the genetic correlation between HW and resistance to TiLV found in the current study is not different from zero, suggests the feasibility of improving both traits independently and that selective breeding for TiLV resistance will not have a negative impact on weight at harvest, or vice versa.

In conclusion, resistance to TiLV as measured by survival during a field outbreak has a significant and high heritability. These results highlight that genetic improvement of TiLV resistance is feasible in a Nile Tilapia breeding population. However, for this trait to be included routinely into breeding programs, a reliable disease challenge model would be very useful, and assessing the genetic correlation between survival in an experimental and a field challenge would be highly informative. Nonetheless, the results herein are highly encouraging for the use of selective breeding to help tackle one of the primary disease concerns for tilapia aquaculture globally. Future studies will be required to evaluate the genetic architecture of host resistance to TiLV, and to evaluate the possibility of marker-assisted or genomic selection to expedite the breeding of tilapia strains with improved resistance to the virus.

Ethics approval and consent to participate

Data collection and sampling was performed as part of a non-profit selective breeding program run by WorldFish. The animals from this breeding population are managed in accordance with the Guiding Principles of the Animal Care, Welfare and Ethics Policy of WorldFish Center.

Consent for publication

Not applicable.

Availability of data and materials

The dataset used in the current study is available from the corresponding author on reasonable request.

Declaration of Competing interests

The authors declare that they have no competing interests.

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Authors’ contributions

AB performed the analysis and wrote the first draft of the manuscript. TT and MM supervised the data measurement and provided the data, MC contributed to the experimental design and veterinary diagnosis, JB and RH conceived the experiment and provided data for analysis. All authors improved the writing, read and approved the final manuscript.

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Appendix A. Supplementary data

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