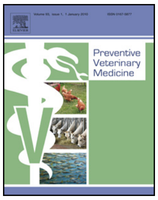
Preventive Veterinary Medicine 115 (2014) 101–108

Contents lists available at ScienceDirect

Preventive Veterinary Medicine

journal homepage: www.elsevier.com/locate/prevetmed



Prediction of province-level outbreaks of foot-and-mouth disease in Iran using a zero-inflated negative binomial model

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ARTICLE INFO

Article history:
Received 10 September 2013
Received in revised form 12 March 2014
Accepted 20 March 2014

Keywords:
Foot-and-mouth disease
Iran
Outbreak
Zero-inflated negative binomial

ABSTRACT

To identify events that could predict province-level frequency of foot-and-mouth disease (FMD) outbreaks in Iran, 5707 outbreaks reported from April 1995 to March 2002 were studied. A zero-inflated negative binomial model was used to estimate the probability of a 'no-outbreak' status and the number of outbreaks in a province, using the number of previous occurrences of FMD for the same or adjacent provinces and season as covariates. For each province, the probability of observing no outbreak was negatively associated with the number of outbreaks in the same province in the previous month (odds ratio [OR] = 0.06, 95% confidence interval [CI]: 0.01, 0.30) and in 'the second previous month' (OR = 0.10, 95% CI: 0.02, 0.51), the total number of outbreaks in the second previous month in adjacent provinces (OR = 0.57, 95% CI: 0.36, 0.91) and the season (winter [OR = 0.18, 95% CI: 0.06, 0.55] and spring [OR = 0.27, 95% CI: 0.09, 0.81], compared with summer). The expected number of outbreaks in a province was positively associated with number of outbreaks in the same province in previous month (coefficient [coef] = 0.74, 95% CI: 0.66, 0.82) and in the second previous month (coef = 0.23, 95% CI: 0.16, 0.31), total number of outbreaks in adjacent provinces in the previous month (coef = 0.32, 95% CI: 0.22, 0.41) and season (fall [coef = 0.20, 95% CI: 0.07, 0.33] and spring [coef = 0.18, 95% CI: 0.05, 0.31], compared to summer); however, number of outbreaks was negatively associated with the total number of outbreaks in adjacent provinces in the second previous month (coef = −0.19, 95% CI: −0.28, −0.09). The findings indicate that the probability of an outbreak (and the expected number of outbreaks if any) may be predicted based on previous province information, which could help decision-makers allocate resources more efficiently for province-level disease control measures. Further, the study illustrates use of zero inflated negative binomial model to study diseases occurrence where disease is infrequently observed.

1. Introduction

Foot-and-mouth disease (FMD) is caused by one of the seven immunologically distinct serotypes of foot-and-mouth disease virus (FMDV) that belong to the *Picornaviridae* family of the *Aphthovirus* genus (Sobrino et al., 2001; Sáiz et al., 2002). FMD mainly affects domestic and wild even-toed ungulates, although it can occur naturally or experimentally in other animals (Davies,

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http://dx.doi.org/10.1016/j.prevetmed.2014.03.018
0167-5877/

2002). FMD can be transmitted by animal-to-animal contact, by mechanical means via vehicles or clothing, and possibly in the air at least for short distances. The different mechanisms of transmission can be influenced by the meteorological and epidemiologic conditions and also by the virus strain, stage of disease, and host species (Donaldson and Alexandersen, 2002; Musser, 2004). Spread of FMD can be extremely rapid because of the extensive amount of virus shed in the sub-clinical stages of disease and of the low infectious dose of virus required for infection (Sutmoller and Casas, 2002; Carpenter et al., 2004).

Currently, there is a global concern about the introduction or transmission of FMD from countries with endemic FMD status to countries that are FMD-free (Rweyemamu and Astudillo, 2002; Crispin, 2005; Knowles et al., 2009). For more than 60 years, FMD has been endemic in Iran (Arshadi and Maldjaii, 1976), which has one of the highest annual rates of FMD outbreaks reported to international organizations, despite the application of vaccination and quarantine (Traub et al., 1966; Kaveh, 1969; Fahrang-Far, 1972; Arshadi and Maldjaii, 1976; Klein et al., 2006). However, there are relatively few studies on FMD in Iran with respect to the factors or events that are contributing to FMD outbreaks or to its endemic status (Perez et al., 2005; Klein et al., 2007; Knowles et al., 2009; Choi et al., 2012; Rashtibaf et al., 2012).

Modeling of FMD can help to understand the dynamics and epidemiology of the disease by identifying and quantifying likely contributing factors. Models also can help to study the behaviors or situations that cannot be evaluated experimentally or are often too resource-intensive or expensive to implement. Disease modeling also can be used to evaluate effectiveness of control or prevention strategies, as well as to identify strategies to reduce economic losses. Thus, in addition to contributing to a better understanding of the biologic processes of the disease and quantifying disease dynamics, modeling, with appropriate interpretation, also can help provoke ideas or provide guidelines for decision-making (Pfeiffer, 2004).

FMD has been a challenging problem in Iran for decades, and recently, models have been developed to address factors associated with transitions between endemic and epidemic conditions (Choi et al., 2012). The purpose of this research was to identify and quantify previous FMD events that may be associated with province-level frequency of FMD outbreaks in Iran, which could be applied to implementation and evaluation of province-level control measures and policies by regional or national veterinary organizations and decision-makers.

2. Methods

In this section, the available data for this study are briefly discussed, followed by a description of data distribution and analytical problems related to count data with an excessive number of observed counts equal to zero. An observed count of zero in this study corresponds to a province and month for which no outbreaks were observed. The modeling approach is described, followed by a description of covariate data.

2.1. Data description

Official monthly-reported outbreaks of FMD in Iran from April 1995 to March 2002 (1374–1380 Iranian calendar year) were obtained from the Iran Veterinary Organization (IVO). To check the accuracy of data when the number of reported outbreak for a province in a given month was zero, the IVO data were compared to the data reported to Office International des Epizooties (OIE). During the study period, the number of provinces in Iran increased from 24 to 28 due to province divisions. To maintain data consistency, when separate data were available, FMD outbreak reports for new provinces, i.e. Ardebil, Golestan, Qazvin, and Qom, were pooled with those of East Azarbayejan, Mazandaran, Zanjan, and Tehran, respectively.

2.2. Distributional assumption and modeling

The distribution of the number of reported outbreaks was highly skewed (Fig. 1) and contained an abundance of zeros because there were no reported outbreaks in some provinces for many months during the study period. A Poisson regression model was considered initially for the count of FMD outbreaks; however, the Poisson regression assumption that the mean and variance are equal did not hold for the data. A model using a negative binomial regression was then considered, which is a natural extension of the Poisson model (Slymen et al., 2006). A negative binomial model allows for the variance to be greater than the mean, as a remedy for over-dispersion. Although the negative binomial model can account for the over-dispersion in the count data, it may not adequately account for the relatively high (compared to an ordinary count model) frequency of zeros for province-months where no outbreak was reported.

Thus, a zero-inflated model was considered, assuming an additional latent (unobserved) data-generating process for ‘excess zeros’, i.e. zeros in excess of what is expected under a regular count model. A zero-inflated model augments the zeros arising from a count distribution and accounts for the probability of excess zeros via extra modeling, such as logistic regression (Lambert, 1992). Thus, a zero-inflated model is a mixture model with a point mass at zero (Appendix A).

The fit of the ordinary count models (Poisson and negative binomial) was compared along with their zero-inflated analogs (zero-inflated Poisson and zero-inflated negative binomial), using the Vuong test, a likelihood ratio-based statistic that measures the distance/closeness between two models (Vuong, 1989). The Vuong test statistic is based on the comparison of the predicted probabilities of the two models and is distributed asymptotically standard normal under the null hypothesis the two models fit the data equally well. A large, positive test statistic provides evidence of the superiority of model 1 (model used in the numerator when calculating the test statistics) over model 2 (model in the denominator), whereas a large, negative test statistic is the evidence of the superiority of model 2 over model 1. Thus, the choice to use an appropriate (zero-inflated versus conventional ordinary count) model was