



Assessing epidemiological parameters and dissemination characteristics of the 2000 and 2001 foot-and-mouth disease outbreaks in Rio Grande do Sul, Brazil

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ABSTRACT: Since 1998, the state of Rio Grande do Sul, Brazil, has been free of foot-and-mouth disease (FMD) with yearly mandatory vaccination until the 2000 and 2001 FMD reintroductions. This study gathered data from both outbreaks from official veterinary state service archives and field investigation reports to quantify epidemiological parameters such as epidemic duration and the number of secondarily infected farms and animals, which are necessary for estimating outbreak dynamics parameters. We applied a Bayesian latent variable approach to estimate the time-varying reproduction number R_t at animal level and calculated the number of newly confirmed cases by infection date. Our results demonstrated that for 2000 outbreaks, with 22 infected farms, the median R_t was just above one, while 2001 outbreaks exhibited a R_t of 1.6, which would explain the wider spread of infection among the 30 infected farms. Our findings not only provide key FMD transmission parameters and highlight the main epidemiological differences between epidemics but also emphasize the practical implications for Brazil's preparedness for future FMD outbreaks, including potential surveillance approaches and guidance for producers. Furthermore, this study demonstrated how high-quality epidemic data can be used to reconstruct past outbreaks contributing to post-epidemic preparedness.

Key words: reproduction number, foot-and-mouth disease, outbreak.

Avaliação dos parâmetros epidemiológicos e características de disseminação dos focos de febre aftosa de 2000 e 2001 no Rio Grande do Sul, Brasil

RESUMO: A partir de 1998, o Estado do Rio Grande do Sul, Brasil, se tornou livre de febre aftosa com vacinação obrigatória anual até as reintroduções da doença em 2000 e 2001. Este estudo reuniu dados de ambos os focos a partir de arquivos do serviço veterinário oficial do Estado e relatórios de investigações de campo, com o objetivo de quantificar parâmetros epidemiológicos, como duração da epidemia e número de fazendas e animais secundariamente infectados, necessários para estimar parâmetros da dinâmica do surto. Aplicamos uma abordagem Bayesiana de variável latente para estimar o número efetivo de reprodução em função do tempo (R_t) em nível animal e calculamos o número de novos casos confirmados por data de infecção. Nossos resultados demonstraram que, nos surtos de 2000, com 22 fazendas infectadas, o valor mediano do R_t foi ligeiramente superior a um, enquanto nos surtos de 2001, o R_t foi de 1,6, o que explicaria a maior disseminação da infecção entre as 30 fazendas afetadas. Nossas descobertas não apenas fornecem parâmetros chave da transmissão da febre aftosa e destacam as principais diferenças epidemiológicas entre as epidemias, mas também enfatizam as implicações práticas para a preparação do Brasil em futuros surtos de febre aftosa, incluindo abordagens potenciais de vigilância e orientações para os produtores. Além disso, este estudo demonstrou como dados de epidemias de alta qualidade podem ser utilizados para reconstruir surtos passados, contribuindo para a preparação pós-epidêmica.

Palavras-chave: número de reprodução, febre aftosa, foco.

INTRODUCTION

Foot-and-mouth disease (FMD) control and eradication are challenging and expensive, mainly because of international trade bans and the direct and indirect costs of control and eradication

activities (JUNKER et al., 2009; KITCHING & ALEXANDERSEN, 2002; PENDELL et al., 2007). The estimated cost of an outbreak in FMD-free countries can exceed US\$ 1.5 billion per year (KNIGHT-JONES & RUSHTON, 2013) and the reintroduction of FMD is predicted to cost

approximately US\$ 47 billion in gross domestic product loss and 677,000 jobs lost would result from a depopulation strategy without vaccination (MILLER et al., 2019).

In 2000, the reintroduction of FMD into South America caused extensive economic and social losses to livestock systems in Argentina, Uruguay and the State of Rio Grande do Sul, Brazil (LYRA & SILVA, 2004; MAPA, 2002). After the spread of FMD to a region considered free of FMD, Brazilian animal health authorities increased surveillance and carried out eradication strategies, which led to outbreak control and elimination (LYRA & SILVA, 2004; MAYEN, 2003). However, in 2001, a rapid and massive epidemic again affected the Prata Basin region (CORREA MELO et al., 2002; LYRA & SILVA, 2004; NARANJO & COSIVI, 2013; PEREZ, et al., 2004). Following these events, the number of outbreaks in South America decreased significantly (NARANJO & COSIVI, 2013) and since 2019, no new outbreaks have been reported in the region, despite Venezuela's absence of official international status for FMD (PANAFTOSA, 2020). In 2021, the state of Rio Grande do Sul, among other Brazilian states, was recognized by the World Organization for Animal Health (WOAH) as an FMD-free zone where vaccination is not practiced (WOAH, 2021).

Historical data are often used for post-epidemic policy and for estimating transmission parameters directly from outbreaks, such as farm-level information, animal populations, husbandry characteristics, and movement patterns (VAN ANDEL et al., 2021). The most used methodologies for estimating epidemic sizes and evaluating the effectiveness of countermeasures are based on mathematical transmission models (KNIGHT-JONES et al., 2016; POMEROY et al., 2017; PROBERT et al., 2018). Outbreak data have been used to estimate the basic reproduction number R_0 (COLENUTT et al., 2020; ESTRADA et al., 2008; FERGUSON et al., 2001; KEELING, 2005; MUROGA et al., 2012; PEREZ et al., 2004; TADESSE et al., 2019), which briefly, represents the average number of secondary infections caused by an infected individual in a completely susceptible population (ANDERSON & MAY, 1992; DELAMATER et al., 2019; DIETZ, 1993). While R_0 is useful for estimating the expected number of new infections in a naïve population, as epidemics propagate, numerous factors directly influence transmission, such as the effect of control measures and the reduction in the availability of susceptible animals (HAYDON et al., 2003; TILDESLEY & KEELING, 2009). Thus, to follow

epidemic propagation over time in a given population, the best metric is the time-varying reproduction number (R_t), which is defined as the average number of secondary cases per primary case at a given time t (CORI et al., 2013; MERL et al., 2009; VEGVARI et al., 2021). Because R_t is estimated from underlying infections, it is important to account for the incubation period and the uncertainty associated with delays between symptoms onset and the date of the case report (ABBOTT et al., 2020; GOSTIC et al., 2020; NAKAJO & NISHIURA, 2022; PROBERT et al., 2018).

This study described and estimated the transmission parameters of the 2000 and 2001 FMD outbreaks in the State of Rio Grande do Sul, Brazil. Here, we used outbreak data to quantify epidemiological parameters such as epidemic duration and the number of secondary infected animals and to estimate the rate of epidemic growth. We applied a Bayesian latent variable approach using back-calculation to estimate the time-varying reproduction number and calculate the number of new confirmed cases by infection date. Ultimately, this study provided a comprehensive understanding of historical events and supported strategic policies based on further transmission models that can be used to investigate future epidemics and the effectiveness of countermeasures.

MATERIALS AND METHODS

FMD outbreak data

This study utilized 2000 and 2001 FMD epidemic data from the state of Rio Grande do Sul, Brazil, Official Veterinary Services archives (SEAPDR-RS, 2021). The databases contained information on field investigation reports produced during and after outbreaks (MAPA, 2002). Data included infected farms' information, such as herd size, geolocation, the chronology of control and eradication events (e.g., first notification, movement restrictions, and vaccination), clinical investigation findings, such as ages of clinical lesions (EUFMD, 2020; KITCHING & ALEXANDERSEN, 2002; MAPA, 2002), the number of daily new infected herds, and the number of susceptible animals by species per farm.

Estimating FMD effective reproduction number

We reconstructed the outbreaks time series to estimate the latent infections I_t at animal level by fitting a back-calculation model (BECKER et al., 1991; WHITE et al., 2009) using daily

infected animals records collected from August 1st to September 22nd, 2000, and from May 5th to July 18th, 2001 (MAPA, 2002; SEAPDR-RS, 2021) as illustrated in figure 1. The infection estimates were mapped to the expected number of reported cases, D_t , given $\mathfrak{Z}$, which represents the convolution of a certain incubation period and reporting delay distributions, which measures the time from infection to reporting. The observed reported case counts, C_t , were ultimately generated from a negative binomial model with mean D_t and overdispersion Φ , sampled from an exponential prior. The time-varying reproduction number R_t was estimated by the ratio of the number of new infections generated at time step t , to the sum of infection incidence up to time $t-1$ weighted by an uncertain generation time function W_s (ABBOTT et al., 2020; 2021; CORI et al., 2013; SHERRATT et al., 2021), as follows.

$$D_t = \sum_{\tau} \mathfrak{Z}_{\tau} I_{t-\tau} \quad (1)$$

$$C_t \sim \text{Negative binomial}(D_t, \Phi) \quad (2)$$

$$R_t = \frac{I_t}{\sum_{s=1}^t I_{t-s} W_s} \quad (3)$$

Here, we used a mean generation time of 6.1 and a standard deviation of 4.6 obtained from the literature (HAYDON et al., 2003). For the incubation period, the mean and standard deviation were drawn from a Poisson distribution with λ equal to 5.9 based on a published meta-analysis (MARDONES et al., 2010). The delays between symptom onset and case reporting for each infected farm were extracted directly from the 2001 FMD outbreak investigation reports (SEAPDR-RS, 2021) and modeled via a log-normal distribution. The parameters used are summarized in table 1. The Bayesian latent variable model was implemented in R version 4.1.1 using the

EpiNow2 package (ABBOTT et al., 2021; R CORE TEAM, 2019). For every model run, four chains were used with a warmup of 500 samples each and 4,000 samples post-warmup.

RESULTS

The reintroductions of FMD in Rio Grande do Sul in 2000 and 2001 were considered independent epidemiological events. The first official notification became public on August 1st, 2000, at the municipality of Jóia, 145 km from the border with Argentina (Figure 2). The outbreak spread into three other neighboring municipalities, Eugênio de Castro, Augusto Pestana, and São Miguel das Missões, in the northwestern region of the state, which was characterized by family or subsistence farming, with a primary focus on milk production and corresponded to a total area of 3,439 km². In 2000, a total of 22 farms (Table 2) were infected and the outbreak was confirmed to be caused by the type O virus (MAPA, 2002). In May 2000, three months before the 2000 outbreak, the Brazilian government implemented changes to FMD sanitary policy for Santa Catarina and Rio Grande do Sul States, including vaccination withdrawal, as a strategy to obtain the WOAHP recognition of those as FMD-free zones where vaccination is not practiced (MAPA, 2000). Control measures were implemented according to the national contingency plans and included establishing surveillance zones, in which animals and animal sub-product movement were restricted, and clinical inspection of susceptible animals was carried out routinely. Within the three kilometers infection zones, susceptible animals on infected farms and their immediate contact farms were culled, followed by cleaning and disinfection procedures and quarantine before repopulating farms (MAPA, 1993). The

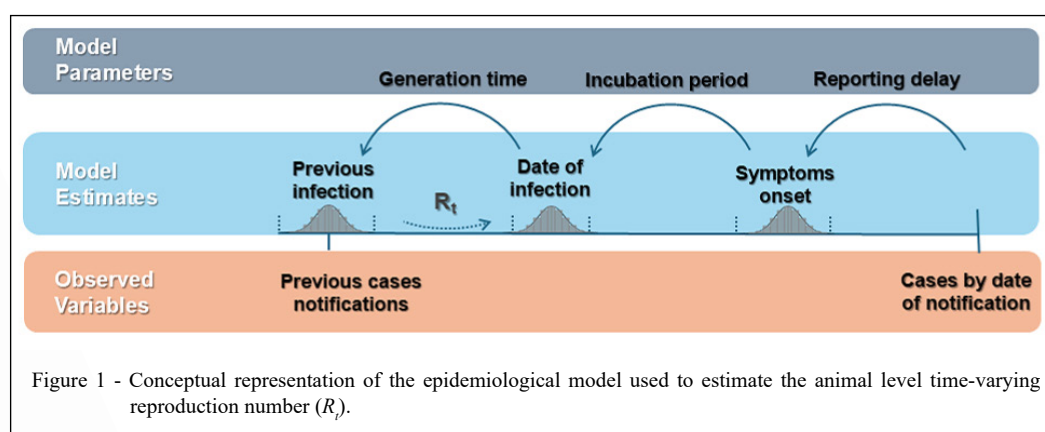


Table 1 - Summary of epidemiological parameters, distributions, and references used in the estimation of transmission dynamics for the 2000 and 2001 FMD outbreaks in Rio Grande do Sul, Brazil.

Model parameter	Value	Reference/Source
Generation time	Mean: 6.1, SD: 4.6	HAYDON et al., 2003
Incubation period	Poisson $\lambda = 5.9$	MARDONES et al., 2010
Reporting Delay	Mean: 5.03, SD: 3.59	SEAPDR-RS, 2021

vaccination forbiddance was sustained in the state even after the outbreak started as a strategy to retain the conditions required to obtain OMSA free from FMD without vaccination zone status (MAPA, 2002). The surveillance activities carried out as part of the activities to substantiate freedom from FMD involved 1,078 farms and 12,795 blood samples. The end of the outbreak was declared in February 2001 and the final cost of the 2000 outbreak was estimated to be US\$ 3,7 million (MAPA, 2002).

Nevertheless, among the numerous FMD outbreaks reported by Argentina and Uruguay animal health authorities (CORREA MELO et al., 2002; IRIARTE et al., 2023; PEREZ et al., 2004; PEREZ et al., 2004), on May 5th, 2001, a new introduction was identified in the municipality of Santana do Livramento, five km from the Uruguay border. Laboratory diagnosis confirmed a type A

virus revealing the absence of an epidemiological link with the 2000 outbreak (MAPA, 2002). The epidemic infected 30 farms in six municipalities, with a predominance of cattle farming aiming milk production, comprising a 27,053 km² area, which included three distinct geographic regions: Santana do Livramento and three contiguous municipalities, Alegrete, Quaraí, and Dom Pedrito, and the municipalities of Jari and Rio Grande, which are 225 km and 412 km from the first notified case, respectively. Table 2 presents a comparison of the 2000 and 2001 FMD outbreaks. The 2001 outbreak was larger, affecting 30 farms, and involved larger median herd size of 187 animals than 2000 outbreak, with 22 farms affected and median herd size of 55.5 animals. The ruminants population experienced a significantly greater impact in 2001 when compared to 2000. Conversely, the swine population was

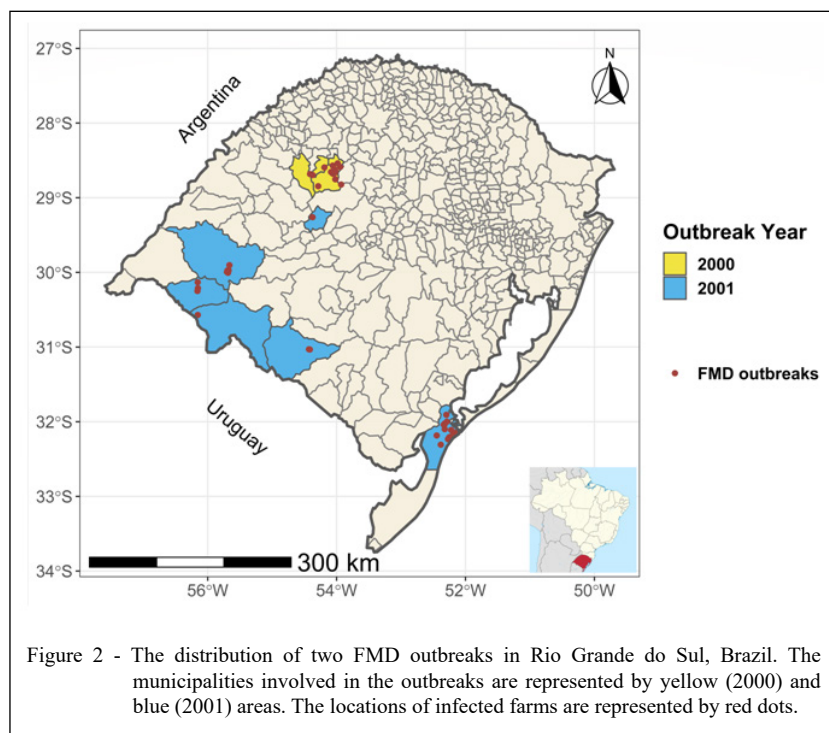


Figure 2 - The distribution of two FMD outbreaks in Rio Grande do Sul, Brazil. The municipalities involved in the outbreaks are represented by yellow (2000) and blue (2001) areas. The locations of infected farms are represented by red dots.

Table 2 - Years 2000 and 2001 outbreak descriptions are based on official veterinary state service archives, databases, and reports produced during and after the epidemic events (MAPA, 2002).

	Foot-and-mouth disease -----outbreaks-----	
	2000	2001
Total number of infected farms	22	30
-----Herd size-----		
Median	55.5	187
Minimum	8	15
Maximum	781	3,528
-----Bovine-----		
Exposed	2,545	11,562
Diseased	90	652
Culled	8,185	11,707
-----Small ruminants-----		
Exposed	317	5,039
Diseased	0	0
Culled	776	5,039
-----Swine-----		
Exposed	266	5
Diseased	20	0
Culled	2,106	5

affected more in 2000, with 20 diseased animals, while no diseased swine were detected in the 2001 outbreak. Furthermore, the age of the oldest clinical lesion in days was characterized for each outbreak farm and used to estimate the reporting delay, defined as the time between symptom onset and notification to authorities. During the 2001 outbreaks, the mean age of the oldest lesion was 5.03 days (SD = 3.59). In the Rio Grande municipality, the mean age of lesions was longer, at 6.94 days (SD = 3.25), while in the remaining municipalities, it was markedly shorter, with a mean of 2.17 days (SD = 1.70). The primary clinical findings in bovines were tongue lesions, followed by lesions on the muzzle and udder. All affected swine had been exposed to bovines during the later phase of the disease (MAPA, 2002).

In addition to the control measures outlined in the contingency plan implemented in the 2000 outbreak, for the 2001 outbreak, animal health authorities established an immediate vaccination for cattle and buffaloes followed by revaccination after 30 to 40 days, with a total of approximately 13.3 million revaccinated animals (MAPA, 2001). Serosurveillance was likewise conducted as part of the control measures but also to recover the status of free from FMD. For the 2001 epidemic, approximately

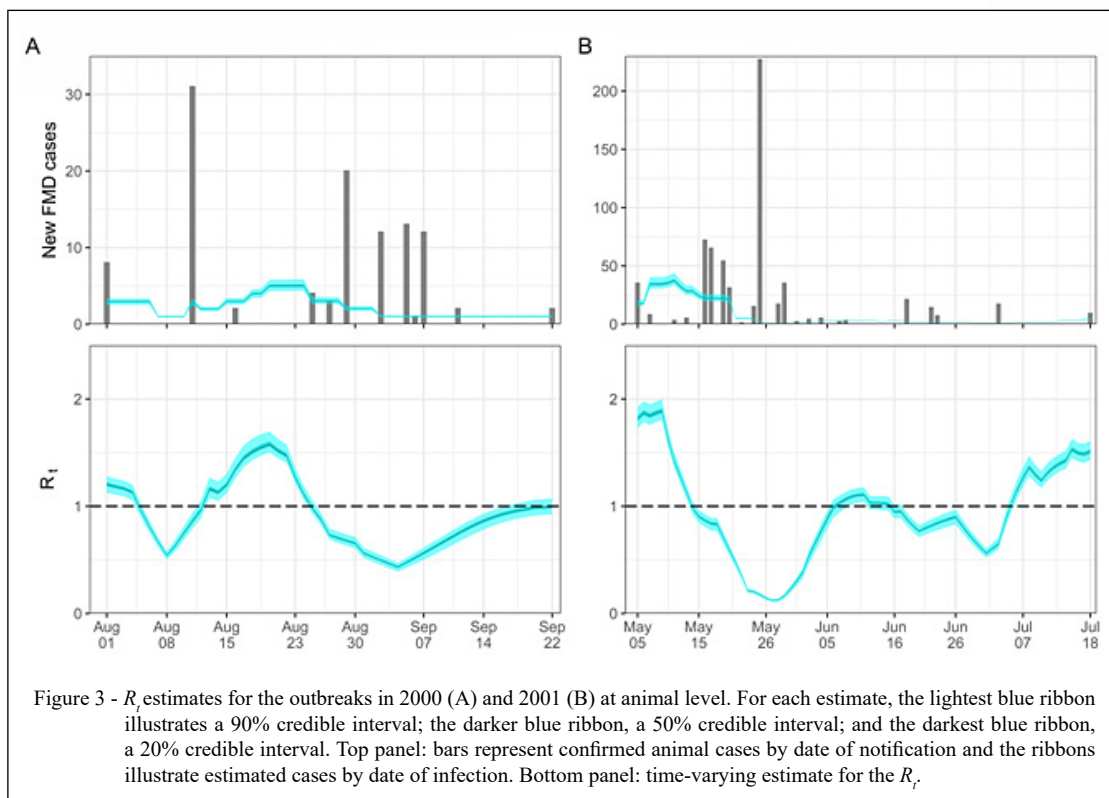
130,000 samples were collected from 1,867 farms. The overall cost of the 2001 outbreak, including indemnities, was estimated at US\$ 7.7 million, and the restrictions imposed to control disease spread were only withdrawn in April 2002 (MAPA, 2002).

The Bayesian latent variable model estimated a median time-varying reproduction number (R_t) of 1.00 (90% CI: 0.93, 1.10) for the 2000 outbreak. The corresponding growth rate yielded to a median value of -0.00051 (90% CI: -0.012, 0.013) while the estimated change in daily cases was near zero, with a median of zero (90% CI: 0, 1), suggesting a stable incidence (Figure 3A). In contrast, the 2001 outbreak exhibited a median R_t of 1.60 (90% CI: 1.50, 1.70), with a corresponding positive median growth rate of 0.088 (90% CI: 0.076, 0.100) and an estimated change in daily cases exhibited a median of three new cases (90% CI: 3, 4), indicating an increase in daily new cases (Figure 3B).

DISCUSSION

Data from the 2000 and 2001 outbreaks were used to estimate disease transmission parameters. The 2000 epidemic was a small-scale outbreak with a median R_t of approximately one, while 2001 was a larger epidemic with sustained transmission demonstrated by a median R_t of 1.6.

According to official reports, the 2000 outbreak was associated with the illegal import of cattle infected with a type O FMD virus from the northern region of Argentina into farms in the municipality of Jóia, 145 km distant from the border (MAPA, 2002). Later studies demonstrated a close genetic relationship between the Argentina virus strain and the ones isolated in Uruguay and Brazil during the same year, suggesting that transboundary movement played an important role in virus dissemination (MALIRAT et al., 2007; MATTION et al., 2004). The type A virus isolated in the 2001 outbreak was also genetically linked with the strains isolated in Uruguay and Argentina (MAPA, 2002), validated by other phylogenetic studies (KÖNIG et al., 2007; MATTION et al., 2004). The main hypothesis about the dissemination of the 2000 outbreak from a single primary case in Jóia to nearby municipalities was attributed to unauthorized cattle movement and indirectly via artificial insemination technicians. A thorough analysis carried out by the authorities of the animal movement records concluded that there was no movement among infected farms, reinforcing the hypothesis of local transmission (MAPA, 2002). The 2000 outbreak was limited to 22 infected farms



in four municipalities. This limited dispersion could be attributed to the low animal density in the infected area. Additionally, dissemination was associated with intense movement of milk tank trucks, and unofficial animal movements between those farms (MAPA, 2002). The residual effect of countermeasures actions and residual herd immunity due to the recent vaccination campaign in 2000 (MAPA, 2000), might have directly restricted the 2000 epidemic which exhibited R_t of one. The limited spread was also observed in a study describing the genetically related type O FMD outbreak in Argentina in the same year (PEREZ et al., 2004).

In the 2001 FMD reintroduction, official outbreak investigation reports identified intense between-farm movement within municipalities and delayed cases notifications by farm owners, particularly in the Rio Grande municipality, as the primary factors contributing to the size of the epidemic (MAPA, 2002). Furthermore, the outbreak occurred about 12 months after the last statewide vaccination campaign (MAPA, 2000), when herd immunity was assumed to be reduced due to waning vaccine effectiveness. The analysis of animal movement records from 2001 concluded that there was no inter-municipality animal movement. The

prevailing hypothesis for the 2001 outbreak posits that each of the six primary cases involved independent introductions, likely resulting from the importation of infected animals from Uruguay into each affected municipality. The Jarí outbreak, located farthest from the dry border with Uruguay (Figure 2), illustrate that hypothesis, as the investigation established a direct association with infected farms in Uruguay through the illegal movement of animals into that municipality (MAPA, 2002).

The model estimates demonstrated that R_t in the 2001 outbreak was 60% greater than in the 2000 outbreak, indicating a sustained increase in disease transmission (ANDERSON & MAY, 1992) consistent with the compounded effects of limited herd immunity, delayed notifications, and intense within-municipality animal movements. In the Argentina 2001 outbreak, the herd reproduction ratio (R_h) had a mean $R_h = 2.4$ (PEREZ et al., 2004). In The Netherlands, the same year, the mean estimate for the period before the first disease notification was $R_h = 2.6$, which decreased to $R_h = 0.71$ after the implementation of the countermeasures (BOUMA et al., 2003). In addition, we observed a sharp decrease in R_t two weeks after the beginning of the 2001

outbreak (Figure 3) which could be explained by the mass emergency vaccination implemented four days after the first case was identified and reported (MAPA, 2001). The effect of vaccination on the decline of the FMD epidemic curve is also demonstrated in other field investigations (ESTRADA et al., 2008; PEREZ et al., 2004; RAWDON et al., 2018) and experimental studies (ORSEL et al., 2005).

Furthermore, our findings highlighted the need for clear communication and education for livestock producers regarding the significance of biosecurity measures (SAYERS et al., 2013), vaccination adherence (KNIGHT-JONES & RUSHTON, 2013; RAWDON et al., 2018), and prompt reporting of suspicious clinical signs (ROCHE et al., 2014). Control measures such as trade restrictions and culling are important in managing FMD outbreaks. They can contribute to reducing the effective reproduction number, a key factor in disease eradication, and significantly influence disease transmission (KÖNIG et al., 2007; MALIRAT et al., 2007; MATTION et al., 2004). By enhancing these aspects, Brazil can further strengthen its defense against future FMD outbreaks, reducing the potential economic and animal welfare consequences associated with this devastating disease.

Our FMD outbreak data was restricted to farm-level demographic information, constraining our ability to evaluate within farm epidemic dissemination and our attempt to reconstruct the dissemination events in the contact network via the between-farm movements of that time. The small FMD epidemic sizes limited the availability of models that could be used to estimate secondary transmission dynamics metrics. Also, the influence of vaccination on the onset of clinical signs can affect the delay in reporting infected cases and; consequently, the parameters of our epidemiological model (ORSEL et al., 2007). We acknowledge that the generation time parameter from HAYDON et al. (2003) reflects herd-level dynamics, while animal-level estimates would be more appropriate. In the absence of published animal-level data, we used this value as a proxy, recognizing potential biases in reconstructing latent infections and the time-varying reproduction number. Future studies on animal-level generation times would improve model precision. Our choice of a Bayesian model and its respective distributions was designed to incorporate prior knowledge and uncertainty, providing a framework to accommodate these variations. Direct comparisons between different outbreaks' reproduction numbers (e.i., R_p , R_o) need to be interpreted with caution due

to the inherent limitations, model assumptions, and how each approach addresses uncertainties around infection dynamics and data biases (ABBOTT et al., 2020; DELAMATER et al., 2019; VAN ANDEL et al., 2021; VEGVARI et al., 2021). Furthermore, the variation of virulence and infectivity between different FMD virus strains, and heterogeneity of host animal species may also have affected the transmission dynamics of the outbreaks we described here, thus having to be taken into account when comparing different events (RUEDA et al., 2015; KITCHING et al., 2006).

CONCLUSION

We revised the 2000 and 2001 FMD outbreaks in the State of Rio Grande do Sul. For the 2000 epidemic, the median R_t was one indication that the epidemic was limited, while for the 2001 outbreak, the median R_t was significantly one; therefore, indicating greater dissemination. We remark that the differences in the serotypes of the virus, the density of the animal population, delayed notification of identified cases, and the unequal levels of immunity could explain the differences in size and duration of the 2000 and 2001 epidemics. Our findings underscore the importance of clear communication and education for livestock producers on biosecurity measures, vaccination adherence, and swift reporting of suspicious clinical signs in strengthening Brazil's defense against future FMD outbreaks.

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DECLARATION OF CONFLICT AND INTEREST

All authors confirm that there are no conflicts of interest to declare.

DATA AVAILABILITY STATEMENT

The data that supports the findings of this study are not publicly available and are protected by confidential agreements, therefore, are not available.

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