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Research article

SPATIOTEMPORAL DISTRIBUTIONS OF FOOT AND MOUTH DISEASE BETWEEN 2010-2019 IN TURKEY

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Foot and mouth disease (FMD) is one of the most contagious diseases of livestock with a significant economic impact affecting most countries in the world over the years. In Turkey, FMD is endemic, but there have not been national studies conducted to analyze spatiotemporal pattern of FMD yet. This study was carried out to identify the spatial and temporal distribution of FMD outbreaks in Turkey from January 2010 to December 2019, to guide the eradication following development of control programs against the disease. Thematic maps were produced to determine FMD sensitive regions and Box-Jenkins time series approach was used to analyze the temporal pattern of FMD. Between these dates, 6698 outbreaks and 246341 cases were reported in Turkey, FMD was recorded multiple times in 96.3% of the provinces (n = 78), and the average incidence of FMD outbreaks at the provincial level was calculated as 8.27/ province year. As result of the spatial pattern of FMD, East and Central Anatolia were determined as the regions where the disease was observed intensely. The time series plot of the data showed a general not very regular trend although there was a downward trend with irregular variations. Although, there was no seasonal effect detected by the decomposition of time series, seasonal peaks in the outbreaks were observed, in the spring (n = 2087, 31.16%). In conclusion, the evaluation of spatial and temporal pattern based on FMD outbreaks that are common in Turkey will contribute to eradication of the disease.

Key words: Foot and mouth disease, Geographic information system (GIS), Outbreak, Spatial, Temporal.

INTRODUCTION

Foot and mouth disease (FMD) is a highly contagious transboundary disease of clove-hoofed animals that affects a large number of domestic and wild species. Due to reduced production and trade limitations on a local and international level, as well as high control expenses around the world, FMD causes significant economic losses [1,2]. FMD virus (FMDV) that causes foot and mouth disease is a member of the *Aphthovirus genus* and the *Picornaviridae family* [3]. The virus is very resistant to

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the environment, may survive for almost a month outside of the host or in animal products, and can be transported over large distances by wind [4]. It can be spread across herds through commercial movements, either directly or indirectly. Pyrexia, lameness, shivering, drooling, and vesicular lesions of the tongue, foot, and teats are the most common clinical symptoms [5,6].

Around the world, FMDV has seven different serotypes: A, O, C, and South African Territories (SAT) 1, SAT 2, SAT 3, and Asia 1. With insufficient cross protection, each serotype contains several biotypical strains, topotypes and genetic lineages [7,8].

The first statistical information about foot and mouth disease in Turkey was published in 1914. A wide variaty serotypes have been isolated and identified so far [9]. Sick and suspicious animals are killed and destroyed by burning or burial following the confirmation of FMD cases. Products such as contaminated meat, milk, and other materials are destroyed. Infected and suspected animals are quarantined. Animals around the infection site are vaccinated. Herd immunity is created when at least 80% of the target population is vaccinated against the disease with intense preventive vaccination programs that take place twice a year. Although all these control measures, the disease is endemic across much of Turkey, but a free zone with immunization exists in continental Europe (Thrace). Turkey has made significant attempts to control the disease through vaccination. Because Turkey serves as a reservoir, thus providing its possible transition to Europe, the European Commission spent €65 million on vaccines in endemic Turkey between 2008 and 2011, with additional financing for vaccination in the free zone [10].

Turkey is a bridge connecting Asia and Europe and is very important in terms of the epidemiology and control of the disease [11]. Because there are animal movements from the eastern parts of the country, especially to the Marmara Region, there is a possibility of the disease spreading to Europe. Controlling epidemic diseases requires detailed epidemiological studies. Besides sero-prevalence studies of the disease within the country, spatiotemporal analysis is also considered to be beneficial for the epidemiology of the disease. Despite sero-prevalence investigations conducted in several regions of Turkey, detailed studies on the spatial and temporal distribution of FMD have not been done. The aim of this study is to determine the spatial and temporal distribution of reported FMD outbreaks in Turkey from January 2010 to December 2019 by conducting a registry-based study, to guide the eradication following development of control programs against the disease.

MATERIALS AND METHODS

Study location

Turkey is located between 36° 42' north latitudes and 26° 45' east longitudes, surrounded by the Black Sea on the north, Aegean Sea on the west and Mediterranean Sea on the south [12]. Turkey is located at the crossroads of Europe and Asia, forming a link between the two continents. Thrace is the name of the European section of the country, whereas Anatolia is the name of the Asian part. It is bordered on the northwest by Greece and Bulgaria, on the east by Georgia and Armenia, and on the south by Iraq and Syria.

Turkey is made up of 7 geographic regions, Marmara, Aegean, Mediterranean, Black Sea, Central Anatolia, Eastern Anatolia, Southeast Anatolia. These regions are divided into 81 provinces.

Data collection

FMD is a disease that requires reporting all cases to the national veterinary authority and internationally to WOAH (World Organization for Animal Health). FMD outbreak and case data were obtained from the World Animal Health Information System (WAHIS) database for the period 2010-2019, which was published publicly. The disease was reported only in domestic species (cattle, sheep and goat) and no disease was recorded in wild species. Outbreak and case definition in Turkey is in accordance with WOAH standards. Outbreak means the occurrence of one or more cases in an epidemiological unit whereas case refers to an individual animal infected by a pathogenic agent, with or without clinical signs.

Data analysis

Maps were produced in order to determine FMD sensitive regions in Turkey. For this purpose, a database based on Geographic Information Systems (GIS) was created. Provincial level shape file (.shp extension) data were used to be implemented in the GIS software for spatial analysis and mapping of outputs. The used data is defined in the WGS 84 EPSG:4326 coordinate reference system. The spatial distribution of FMD outbreaks and cases over the study period was drawn using open source QGIS version 3.10.2 software. Descriptive methods were used to calculate the outbreak incidence. The mean FMD outbreak incidence was calculated by summing all reported FMD outbreaks over the study period in Turkey divided by the total number of provinces and number of years. All analyses were conducted using SPSS 23.0 software and EViews 10 Enterprise Edition.

Box-Jenkins time series approach was used to analyze the temporal pattern of FMD. Foremost, time series of the data was plotted for the study period (2010 January-2019 December) to identify the various time series components in the data and the stationarity of the series was investigated. Because this approach necessitates the existence of a stationary time series. Several approaches for testing the stationarity of time series data have been developed in the literature [13,14,15]. The Augmented Dickey- Fuller (ADF) test [16] and the Phillip-Perron (PP) test [17] were used to test the series stationarity in this study. Secondly, to determine the orders p and q of autoregressive model (AR) and moving average model (MA), respectively, an Autocorrelation Function (ACF) and a Partial Autocorrelation Function (PACF) were plotted. p is the degree of the autoregressive model (AR), q is the degree of the moving average model (MA) [18].

Autoregressive (AR) model; the current value of a variable Yt is determined by the values of the p previous values of the variable and an error term. An AR model of order p, known as AR (p), can be expressed as [18,19,20]:

$$Y_t = \mu + \varphi_1 Y_{t-1} + \varphi_2 Y_{t-2} + \varphi_3 Y_{t-3} + \ldots + \varphi_p Y_{t-p} + \varepsilon_t$$

where Y_t represents the current value of the series, $Y_{t-1}, Y_{t-2}, Y_{t-3}, \ldots, Y_{t-p}$ expression the previous values of the same series, $\varphi_1, \varphi_2, \varphi_3, \ldots, \varphi_p$ to indicate the regression coefficients that indicate the effect of previous values on the current value, ε_t denotes a white noise disturbance term that is unaffected by the response variable's previous values.

Moving average (MA) model; If a time series is a weighted linear sum of the last q random shocks/errors, it is said to be a moving average process of order q. The moving average process of order q, known as MA (q), can be expressed as [20,21,22]:

$$Y_t = \mu + \varepsilon_t - \theta_1 \varepsilon_{t-1} - \theta_2 \varepsilon_{t-2} - \theta_3 \varepsilon_{t-3} - \ldots - \theta_q \varepsilon_{t-q}$$

where Y_t represents the current value of the series, $\varepsilon_t, \varepsilon_{t-1}, \varepsilon_{t-2}, \varepsilon_{t-3}, \ldots, \varepsilon_{t-q}$ to indicate white noise, $\theta_1, \theta_2, \theta_3, \ldots, \theta_q$ denotes the regression coefficients of the model.

ARMA (p, q) process that blend both the AR with order p and MA with order q expressed in the equation:

$$Y_t = \mu + \varphi_1 Y_{t-1} + \varphi_2 Y_{t-2} + \varphi_3 Y_{t-3} + \ldots + \varphi_p Y_{t-p} + \varepsilon_t - \theta_1 \varepsilon_{t-1} - \theta_2 \varepsilon_{t-2} - \theta_3 \varepsilon_{t-3} - \ldots - \theta_q \varepsilon_{t-q}$$

Finally, the parsimonious principle was used to identify the models in this study. This principle states that the model with the fewest number of parameters should always be chosen to offer an appropriate representation of the underlying time series data. Information criteria such as Akaike information criterion (AIC) and Bayesian information criterion (BIC) were used to select the best forecasting model that offers the best outcomes for the period 2010-2019, and forecasts were created using this models [23].

RESULTS

Spatial pattern of FMD

Between 2010 and 2019, 6698 FMD outbreaks were reported in Turkey, with an average and median of 669.8 and 614 outbreaks per year respectively. FMD was recorded multiple times in 96.3% of provinces (n = 78) and all geographical regions (n = 7) during this time period. Central Anatolia (24.66%) and East Anatolia (22.19%)

region account for the vast majority of the outbreaks. The average incidence of FMD outbreaks at province level was 82.69/10 province years or 8.27/ province year. On the other hand, when the number of FMD cases was evaluated, a total of 246341 cases were identified, with an average and median of 24634.1 and 18324 cases per year respectively. East Anatolia (36.36%) and Central Anatolia (24.93%) region account for the vast majority of the cases. As a result, while the number of outbreaks was higher in Central Anatolia than in East Anatolia, the number of cases was higher in East Anatolia than Central Anatolia. The temporal, regional and seasonal distribution of FMD epidemics and cases in Turkey between 2010 and 2019 is shown in Table1, the total number of outbreaks and cases at the provincial level is shown in Figure 1, and the mean distribution was shown in Figure 2. In addition, as a result of calculating the average cases per epidemic, it was determined intensely in the eastern and southeastern borders of Turkey (Figure 3).

Table 1. FMD outbreaks and cases by year, geographical region and season over the period 2010-2019.

Year	**Outbreaks**		**Cases**	
	n	**%**	**n**	**%**
2010	1196	17.86	61720	25.05
2011	1267	18.92	40719	16.53
2012	772	11.53	18254	7.41
2013	1193	17.81	51474	20.90
2014	253	3.78	6590	2.68
2015	570	8.51	8668	3.52
2016	658	9.82	22752	9.24
2017	315	4.70	13739	5.58
2018	392	5.85	18393	7.47
2019	82	1.22	4032	1.64
Region	**n**	**%**	**n**	**%**
Mediterranean	573	8.55	10670	4.33
Eastern Anatolia	1486	22.19	89581	36.36
Aegean	843	12.59	25131	10.20
Southeastern Anatolia	198	2.96	10973	4.45
Central Anatolia	1652	24.66	61409	24.93
Black Sea	1371	20.47	37898	15.38
Marmara	575	8.58	10679	4.34
Season	n	%	n	%
Spring	2087	31.16	82308	33.41
Winter	1787	26.68	49123	19.94
Autumun	1140	17.02	41479	16.84
Summer	1684	25.14	73431	29.81

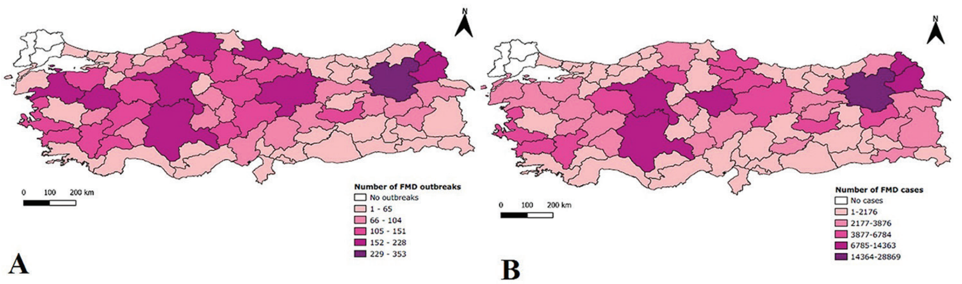

Figure 1. Distribution of FMD outbreaks **(A)** and FMD cases **(B)** in Turkey over the period 2010–2019 (at province level).

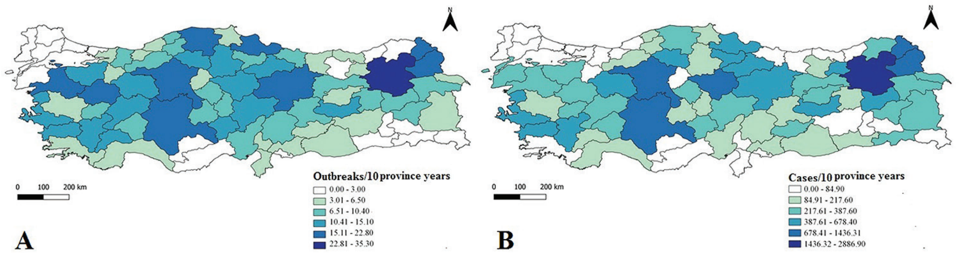

Figure 2. The mean distribution of FMD outbreaks and cases in Turkey over the period 2010-2019 (at province level).

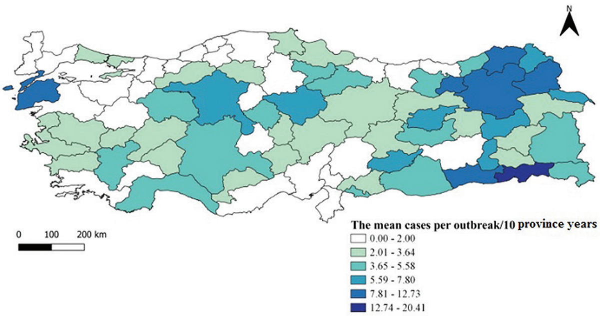

Figure 3. The mean cases per outbreak of FMD in Turkey over the period 2010-2019 (at province level).

Temporal pattern of FMD

In the period from January 2010 to December 2019, a high number of FMD outbreaks was reported in 2011 (n = 1267 outbreaks), 2010 (n = 1196) and 2013 (n = 1193) while the lowest number of outbreaks was reported in 2019 (n = 82) (Table 1). The highest numbers of outbreaks were reported in the month of May (n = 827), which accounted for 12.35% of all reported outbreaks and the lowest in October (n = 333), accounting for 4.97% of all reported outbreaks.

The monthly distribution of FMD outbreak and case series during the study period was shown by the time series graph. As a result of the decomposition with TRAMO/SEATS method of these series., it was determined that there was no seasonal effect [24,25]. For this reason, it has been determined that it is not appropriate to make seasonal decomposition into time series and the observed, final trend cycle and de-trended series were obtained (Figure 4).

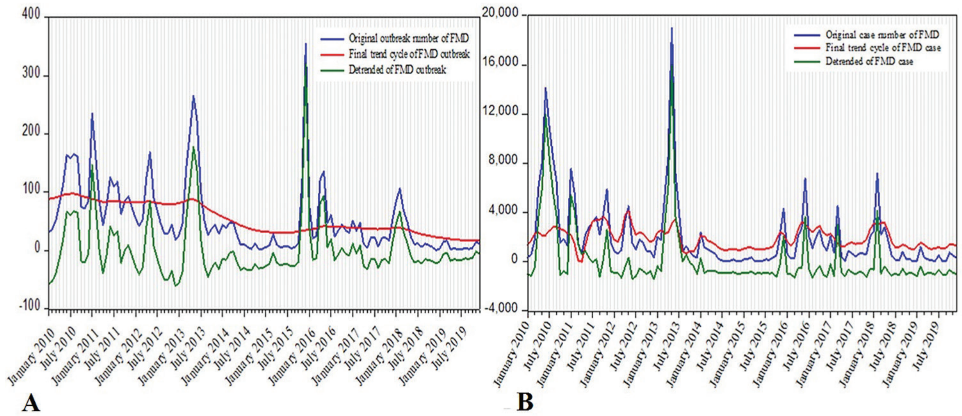

Figure 4. Time plot of the outbreak series (A) and the case series (B) over the period 2010–2019.

Model diagnostics

Before attempting to fit an appropriate model, the time series under consideration should be examined for stationarity. That is, variables must be checked for the presence of unit roots, and the integration order for each series must be decided [26]. The null hypothesis that the series has a unit root problem was imposed first, versus by the alternative hypothesis that the series is stationary. As a result of Augmented Dickey-Fuller test (ADF) and Phillip Perron (PP) tests, it was decided that the series is stationary (Table 2).

In addition to the stationarity tests for the series, the autocorrelation function (ACF) and partial autocorrelation function (PACF) graphics were evaluated in an attempt to determine the AR(p) and MA(q) values required to develop a forecast model. As a result of evaluating the lag numbers in ACF and PACF graphics, the eight combinations specification AR (0-2) and MA (0-2) were considered. Comparison of various AR (p), MA (q) and ARMA (p, q) models were performed and the one with smallest information criteria was selected. Of the models considered, the AIC and BIC statistics confirmed that ARMA (0,2) and ARMA (1,0) model for reported outbreak and cases series had the minimum information criteria respectively. The maximum likelihood method is commonly used to estimate parameter estimates for Box-Jenkins models. As a result, we estimated the parameters for our series using the maximum likelyhood estimation method (Table 3). The graphs of ACF and PACF showed that in selected models the residual error sequence was a white-noise sequence (Figure 5).

Table 2. Augmented Dickey Fuller and Phillips Perron test for the outbreak and case series (at level).

Variable	ADF				PP			
	Trend and Intercept		Intercept		Trend and Intercept		Intercept	
	t-statistic	P-value	t-statistic	P-value	t-statistic	P-value	t-statistic	P-value
FMD outbreaks	-6.47	0.0000	-4.69	0.0002	-5.12	0.0003	-4.64	0.0002
FMD cases	-5.44	0.0001	-4.81	0.0001	-5.24	0.0002	-4.85	0.0001

Table 3. Maximum likelihood parameter estimates for ARMA (0,2) and ARMA (1,0) models for the series.

Variables	Variable	AIC	BIC	Coefficient	Std. Error	t-Statistic	Prob.
Outbreak	C	10.48	10.57	55.36	14.93	3.71	0.0003
	MA(1)			0.78	0.06	13.33	0.0000
	MA(2)			0.44	0.07	6.07	0.0000
Case	C	18.26	18.33	1996.72	962.25	2.08	0.0402
	AR(1)			0.67	0.04	15.26	0.0000

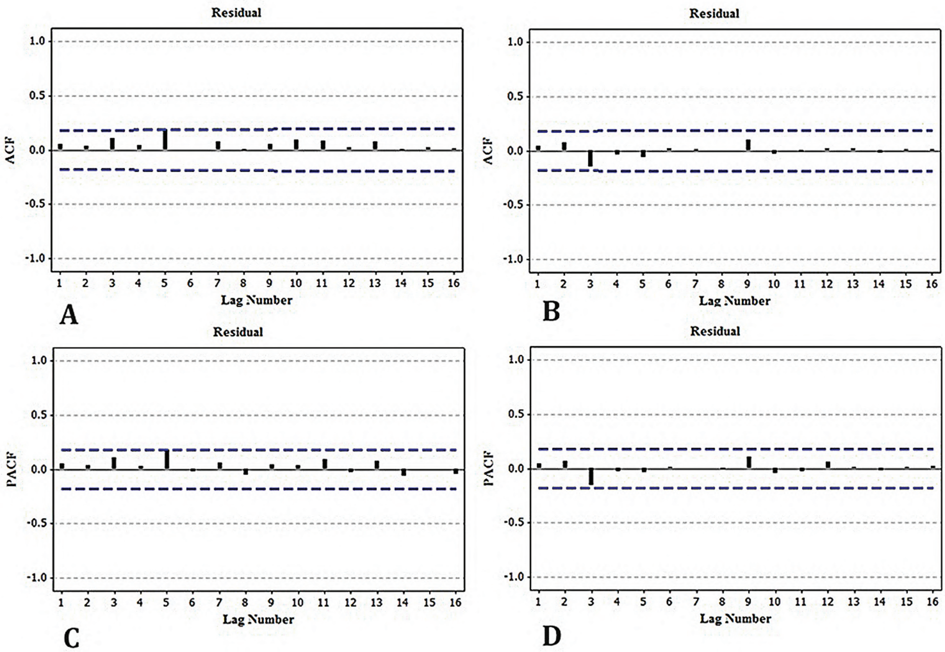

Figure 5. Autocorrelation function (ACF) and partial autocorrelation function (PACF) of outbreak series **(A,C)** and case series **(B,D)** for residual series.

DISCUSSION

Unlike several earlier FMD studies in Turkey that were sero-prevalence studies, this study is the first longitudinal study to report the spatial and temporal distribution of FMD outbreaks in Turkey. Turkey has historically been a high-risk region for outbreak diseases such as foot and mouth disease (FMD), lumpy skin disease (LSD), sheep and goat pox (SGP), and peste des petits ruminants (PPR). Especially, although the Eastern Anatolia region has a good animal husbandry potential, it is one of the regions where the most structural problems are experienced [27]. In addition, it is a region that needs special attention because it is a region where animal movements are intense.

In this study as result of spatial pattern of FMD, East Anatolia and Central Anatolia regions were determined as the regions where the disease was observed intensely. In a number of studies evaluating FMD, it was stated that similarly the Eastern Anatolia region is at risk. Askaroğlu stated in the report he presented to FAO that there are active outbreaks provinces in these regions [28]. Also in another study Branscum et al. expressed that there is an increasing trend in the occurrence of FMD in eastern Turkey [29]. The active and intense continuation of the epidemic in these regions in our study shows that it coincides with this information.

The importance of animal movements on epidemic diseases is widely accepted and there are international regulations exist to reduce the risks. Despite these rules, epidemics occur on a regular basis as a result of both legal and illegal animal movements [30]. In a study evaluating animal husbandry in Turkey, it was stated that there were important animal movements from Erzurum province in the Eastern Anatolia region to large consumption centers in Turkey, illegal animal movements abroad, and as a result, outbreaks were intense [31]. As a result of the evaluation of 10 year FMD data in our study, the highest number of outbreaks and cases observed in Erzurum is compatible with this detection.

The results of our study showed that more than one FMD outbreak was reported in 78 provinces between 2010 and 2019 (except Edirne, Kırklareli, Tekirdag in the Thrace region). Gilbert et al. stated in their study that there were outbreaks in 80 provinces (all provinces except Thrace region) between 1990 and 2002 [32]. In another study, it was stated that although FMD was eliminated from the Thrace region in 2010, it is endemic in Anatolian Turkey [33]. The occurrence of FMD in all geographical regions in our study confirms that it is endemic in Anatolian Turkey.

This study also evaluated the temporal patterns of FMD using outbreak data in Turkey. In temporal pattern evaluation a total of 6698 FMD outbreaks has determined between 2010 and 2019. Similarly, it was stated that 6112 FMD outbreaks were reported to TurkVet in a 10 year period, in compliance with our study [33]. In our study in Turkey FMD was recorded multiple times in 96.3% of provinces (n = 78) between 2010 and 2019 and the average incidence of FMD outbreaks at the province level was 8.27/ province year. In a study conducted in a different country, FMD was reported at least once in 58.5% of the provinces (n = 79), with a lower rate, and the average incidence of FMD outbreaks at province level was 0.26/ province year [34]. According to our study, FMD disease outbreaks, which are commonly detected every year in Turkey, were determined as 246341 cases in the last 10 years, with the highest number reported in 2010. In a similar study evaluating a 10-year period, the highest number of cases was reported in 2011 and then in 2010, with a total of 163733 cases from 2007 to 2017 [1].

The time series plot of the data showed a general not very regular trend although there was a downward trend with irregular variations. Although the series showed a sudden decrease after 2013, it showed a fluctuating course. Thus, there was no clear evidence of a trend in the series. Both the ACF and PACF tailed off to zero indicating stationarity of the outbreak series and the case series. Stationarity tests using the original data showed the outbreak and case series was stationary, implying that the mean of the FMD data is independent of time. This is an evidence of the lack of apparent trend in the series of the outbreak data. These findings are consistent with the findings reported by Gilbert et al. who concluded that although the incidence of FMD has decreased, the disease continues to exist in the country [32]. There was no clear evidence of a trend in the series mentioned in our study, and this trend is not homogeneous across the country as reported in previous studies [29]. Generally, in Turkey, the number of FMD outbreaks does not significantly cycle. On the other hand, previous studies from other endemic countries indicated the epidemic cycle range of three to 6 years [35,36,37].

Generally, FMD is not known to exhibit seasonality, yet several studies have investigated the seasonal effect of FMD using time series analysis showing variations with peaks in different seasons. In a study, using time series analysis, it was clear that outbreaks occurred the highest in March (the dry season) and the lowest in August (the rainy season) [34]. Our study showed that decomposition with TRAMO/SEATS method of time series, determined that there was no seasonal effect. But during the time periods 2010–2019 seasonal peaks in outbreaks were observed, in the spring (n = 2087, 31.16%). Abdrakhmanov et al. stated in their study that similarly the disease increased in spring [38]. On other hand, in a study conducted in Vietnam, it was stated that, in general, most cases were observed in the dry season (November to March), except in the central highlands [1]. As a result, in our study, although the highest epidemic was observed in the spring season in Turkey, approximately the highest epidemic was observed in the dry season (n = 1787, 26.68%) after the spring season.

Animal breeding practices in Turkey, where animals are relocated from enclosed holdings to wide pastures in the spring, may be responsible for the observed patterns of seasonality defined by incidence peaks during spring. Although increased movement may be a factor in spring outbreaks, there are other factors to consider, such as the birth of sensitive animals. Due to the birth of young animals, this results in widespread contact on common rangelands and possibly an increase in the density of the susceptible population. Another possible reason of the spring incidence increase is poor vaccine storage conditions over the winter months, which might have exposed it to cold and resulted in its loss of activity.

There was no trend nor seasonal changes in the time series data of FMD outbreaks and cases in Turkey. Irregular or random fluctuations were observed in the 10 year data studied. The FMD data was best modelled with ARMA (0,2) and ARMA (1,0). The model equation to estimate the expected monthly FMD outbreaks in Turkey produced an MA(1) coefficient of 0.78 plus an MA(2) coefficient of 0.44 with a constant value of 55.36. The model equation to estimate the expected monthly FMD cases in Turkey produced an AR(1) coefficient of 0.67 with a constant value of 1996.72. This is essential for developing a hypothesis to explain the dynamics of FMD occurrence so as to plan prevention programs, optimal use of resources and effective service delivery.

Using historical data on FMD incidence in Turkey, our study demonstrates that quantitative methods for analysis of spatiotemporal data can effectively evaluate the trends of local epidemic formation. As a result, FMD is wide spread and well established in Turkey. It occurred in all regions and almost all of the provinces in country experienced at least one FMD outbreak in the time between 2010 and 2019. The importance of a systematic approach has emerged before, during and after the eradication program. It has also been concluded that the improvement of prevention and control strategies for FMD in endemic countries is necessary.

Authors' contributions

TB collected and organized FMD outbreak data, drafted the manuscript, performed the statistical analysis and wrote the article. ISG participated in the design of the study and has given final approval for the version to be published.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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PROSTORNA I VREMENSKA DISTRIBUCIJA SLINAVKE I ŠAPA U TURSKOJ U PERIODU OD 2010-2019

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Slinavka i šap (SIŠ) je veoma kontagiozna bolest koja ima značajne ekonomske posledice u zemljama gde je prisutna. U Turskoj, SIŠ je endemska bolest, ali još uvek nisu sprovedene nacionalne studije koje bi analizirale njen prostorno-vremenski obrazac. Ova studija je sprovedena kako bi se identifikovala prostorna i vremenska distribucija izbijanja SIŠ-a u Turskoj od januara 2010. do decembra 2019. godine, sa ciljem sprovođenja iskorenjivanja nakon razvoja programa kontrole bolesti.Napravljene su tematske mape za određivanje regiona osetljivih na SIŠ, a pristup vremenske serije Bok-Jenkinsa je korišćen za analizu vremenskog obrasca. U navedenom periodu, u Turskoj je prijavljeno 6698 epidemija sa 246341 slučajeva. SIŠ je zabeležena više puta u 96,3% provincija (n = 78), a prosečna incidencija izbijanja SIŠ-a na nivou pokrajine izračunata je kao 8,27 po provinciji godišnje. Kao rezultat prostornog obrasca, istočna i centralna Anadolija su određene kao regioni u kojima je bolest intenzivno primećena.

Grafikon vremenskih serija podataka pokazao je opšti ne baš pravilan trend, mada je postojao opadajući trend sa nepravilnim varijacijama. Iako dekompozicijom vremenskih serija nije detektovan sezonski efekat, uočeni su sezonski vrhunci izbijanja,i to u proleće (n = 2087, 31,16%). U zaključku, procena prostornog i vremenskog obrasca zasnovanog na epidemijama SIŠ-a koje su uobičajene u Turskoj mogu doprineti iskorenjivanju bolesti.