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RESEARCH ARTICLE

Seasonal Variation and Spatial-Temporal Pattern Analysis of Anthrax among Livestock in Türkiye, 2005-2019

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ABSTRACT

Anthrax has recently re-emerged worldwide, is a notifiable zoonotic disease with a high disease burden in Türkiye. Despite its importance for public health and the economy, little is known about the seasonal and spatiotemporal patterns of anthrax in animals. Therefore, seasonal and spatiotemporal patterns of livestock anthrax were evaluated in this study. At the provincial level, cartographic maps showing the distribution of anthrax outbreaks and cases were created. The spatial autocorrelation function (Moran's I) was employed to assess the spread features of outbreaks and the cluster locations were determined using LISA, Getis-Ord GI*. Using the Chi-square test, proportions of anthrax were calculated, along with their corresponding 95% confidence intervals. Monthly outbreaks were analyzed by the TRAMO/SEATS methods. The anthrax cases exhibited a positive spatial correlation and especially significant clusters were detected in Eastern Anatolia region. Years, regions, species and season were significantly associated with anthrax ($P<0.001$). Between 2005 and 2019, the most outbreaks (160, 10.36%) were recorded in 2018, while the most cases (1702, 15.92%) were recorded in 2005. When evaluated regionally, the highest rate of outbreaks (705, 45.66%) and cases (4539, 42.47%) were recorded in the Eastern Anatolia region. Additionally, the highest rate of outbreaks (631, 40.87%) and cases (4537, 42.45%) were recorded in the summer season. When evaluated in terms of species, the highest number of cases (5314, 49.72%) were recorded in cattles. The outbreak series were decomposed by the TRAMO/SEATS method and it was determined that there was a seasonal effect. When the outbreaks were evaluated on a monthly basis, it was observed that the outbreaks peaked in August (296, 19.17%). In conclusion, the anthrax in Türkiye has been characterized significantly seasonal and spatiotemporal. The disease pattern and obtained findings will contribute in the prevention and control of the disease.

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INTRODUCTION

Anthrax is an acute, infectious disease caused by the spore-forming soil bacterium *Bacillus anthracis* (Beyer and Turnbull, 2009). Anthrax spores have the ability to survive for a very long time, as they are highly resistant to high temperatures, humidity, radiation and chemical agents. Therefore, once absorbed, spores can then mature and regenerate the infection circle (Tekin *et al.,* 2015).

Anthrax is mainly a disease of herbivores and most vulnerable species among mammals are cattle, sheep and goat (Chen *et al.,* 2016; Abdrakhmanov *et al.,* 2017; Lepheana *et al.,* 2020; Zorigt *et al.,* 2021). Additionally, anthrax in wildlife also has been detected (Turner *et al.,* 2013). Infection of humans generally occurs as a result of direct or indirect contact with infected animals or their contaminated products during agricultural activities. Clinical indicators can range in severity from modest to severe and generally include high fever, bleeding from natural orifices, bloating, sudden death, and breathing difficulty (Beyer and Turnbull, 2009; Tekin *et al.,* 2015).

Despite having a global distribution, anthrax has a lower prevalence in most developed countries due to programs for livestock vaccination and other health precautions, but it is still a problem in less developed agricultural societies (Nderitu *et al.,* 2021). Anthrax outbreaks occur more frequently in areas with soil conditions such as high temperature and high humidity, rich calcium, slightly alkaline or neutral and high organic content (Hugh-Jones and Blackburn, 2009; Abdrakhmanov *et al.,* 2017).

Anthrax continues to be reported in many countries of the world, is generally sporadic in Türkiye and has reached an endemic level in some regions. It has been observed that a limited number of studies have been conducted on animal anthrax in Türkiye. Studies are generally more about case definition and anthrax cases seen at certain intervals (Tekin *et al.,* 2015; Demiraslan *et al.,* 2017). In many studies, it has been emphasized that anthrax maintains its importance, especially in the Eastern Anatolia region, and that in addition to vaccination to prevent the disease, awareness of animal breeders, implementation of hygiene and disinfection rules and more radical measures should be taken (Kirecci *et al.,* 2011; Durmaz *et al.,* 2012).

This study is focused to undertake a comprehensive historical epidemiologic investigation on the disease patterns and seasonal variation of livestock anthrax in Türkiye in order to guide the creation of control plans against the disease and, ultimately, the eradication of the disease. Evaluating the patterns of the disease for the first time in Türkiye will be a fundamental study for future research on anthrax. Also, the findings of this study will serve as a foundation for the creation of a spatio-temporal risk-based strategy for the management of anthrax and the creation of regulations that can lessen the disease's negative effects on public health.

MATERIALS AND METHODS

Study area: Türkiye is a country with an area of 780,580 km^2, located the northern hemisphere (Dizman and Mukhtarli, 2021). Its geographic location is situated at 26° and 45° East longitude and 36° to 42° North latitude. It connects the two continents by being situated at their intersection with Asia and Europe. Both the European and Asian parts are known as Thrace and Anatolia, respectively. Türkiye shares borders with Georgia and Armenia to the east, Iraq and Syria to the south, Greece and Bulgaria to the northwest. Mediterranean, Black Sea, Marmara, Aegean, Eastern, Southeastern and Central Anatolia are the seven geographic regions that make up Türkiye. The country has 81 provinces spread over seven regions.

Sources of data: Anthrax is a disease that is obligated to notify the WOAH (World Animal Health Organization) by the veterinary services of member countries. Publicly published World Animal Health Information System (WOAH-WAHIS) records were used to find data on anthrax outbreaks and cases. The compiled half-yearly reports were created usable for study. The data of the research consists of reports between January 2005 and December 2019.

Spatial analysis: A Geographical Information Systems (GIS) based database was created and cartographic maps were produced to identify anthrax susceptible regions at different periods (2005-2009; 2010-2014; 2015-2019) in Türkiye. Provincial level shapefile (.shp extension) data were used. Spatial distribution of anthrax epidemics was plotted using QGIS software (3.10.2 version, open source) in the WGS 84 EPSG:4326 geographical coordinate system.

Also, the distribution properties of outbreak areas are examined using the spatial autocorrelation function (Moran's I). The cumulative anthrax cases per 100,000 livestocks in Türkiye were investigated with global spatial autocorrelation applying a univariate variables exploratory analysis of the spatial data. To identify the locations of the clusters, two distinct techniques (local indicators of spatial association and Getis-Ord GI*) were used and analysis was done using GeoDa (version 1.14) (Anselin, 1995; Anselin *et al.,* 2006).

The rates of anthrax outbreaks by years, regions and seasons and the corresponding 95% confidence intervals were calculated. The relationship among anthrax outbreaks and years, regions, and seasons was examined using the chi-square (X^2) test. For cases of anthrax, same testing was conducted. Analyses were employed using SPSS 23.0 software.

Time series analysis: Time series graph of the original anthrax outbreak data was plotted. The TRAMO/SEATS method, an improved seasonal adjustment tool parallel to the ARIMA model decomposition, was used to assess seasonality in anthrax outbreaks. The outbreak data was decomposed into fundamental components: trend, seasonal factor, and irregular noise. The time series' long and medium-long-term variability, including changing trends (up or down) and significant breakpoints, is the trend component. It depicts fundamental and major trend of a disease. The seasonality component is viewed as a variation that occurs consistently in the same month or quarter every year; indicates the disease's seasonal feature. After subtracting the trend and seasonal factor from the time series, the residual component is known as the irregular noise component (Yang *et al.,* 2014). Time series analyses was employed using EViews 10 Enterprise Edition.

RESULTS

Spatial pattern of anthrax: Anthrax outbreaks (n=1544) were recorded at seventy-six provinces (93.83%, n = 76) and seven geographical regions between these dates. The most outbreaks were seen in Erzurum province (Fig. 1). With an average of 102.93 outbreaks each year in Türkiye, there were a total of 1544 anthrax outbreaks reported between 2005 and 2019. The average number of anthrax outbreaks per provincial was 1.27 per province year or 19.06 /15 province years. When the number of anthrax cases was analyzed, 10688 cases were detected, with an average of 712.53 each year. The average number of anthrax cases per provincial was 8.80 per province year or 131.95 /15 province years. The mean distribution of outbreaks and cases at the provincial level was shown at different periods of analysis (Fig. 2).

The autocorrelation analysis of the cumulative anthrax cases number per 100,000 livestocks in three time frames (2005–2009; 2010–2014; 2015–2019) were tested, and the Moran's I scatter plot of each time frames was produced (Fig. 3). Three-time interval's Moran I indices were all greater than 0, showing that anthrax cases had a positive geographical association and that epidemic zones exhibited spatial clustering. The standard statistics Z are 4.4425, 4.9681 and 3.4635, respectively ($P<0.05$).

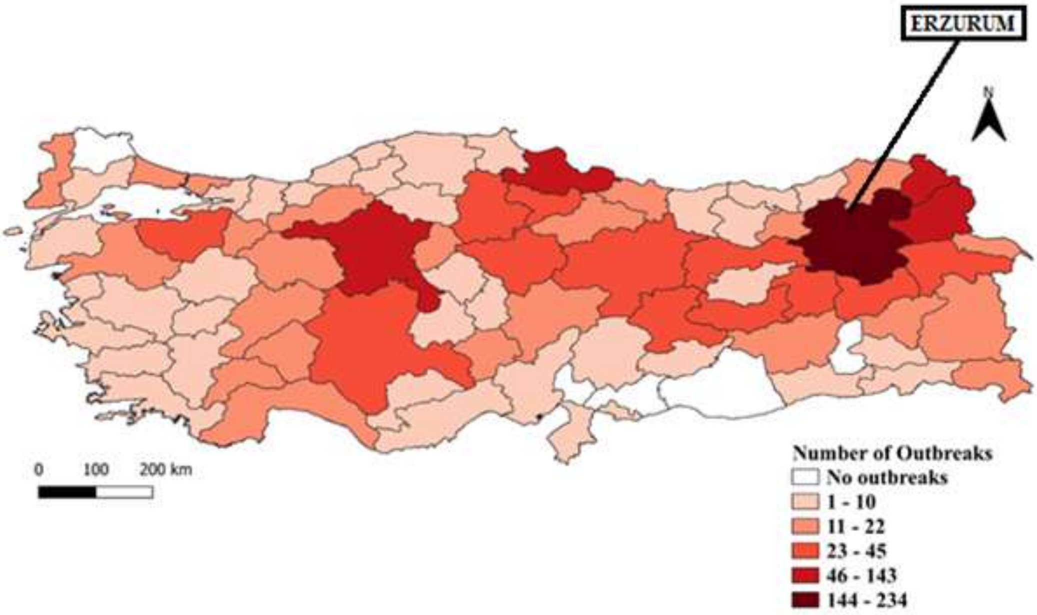

Fig. 1: Distribution of anthrax outbreaks in Türkiye over the period 2005-2019 (at province level)

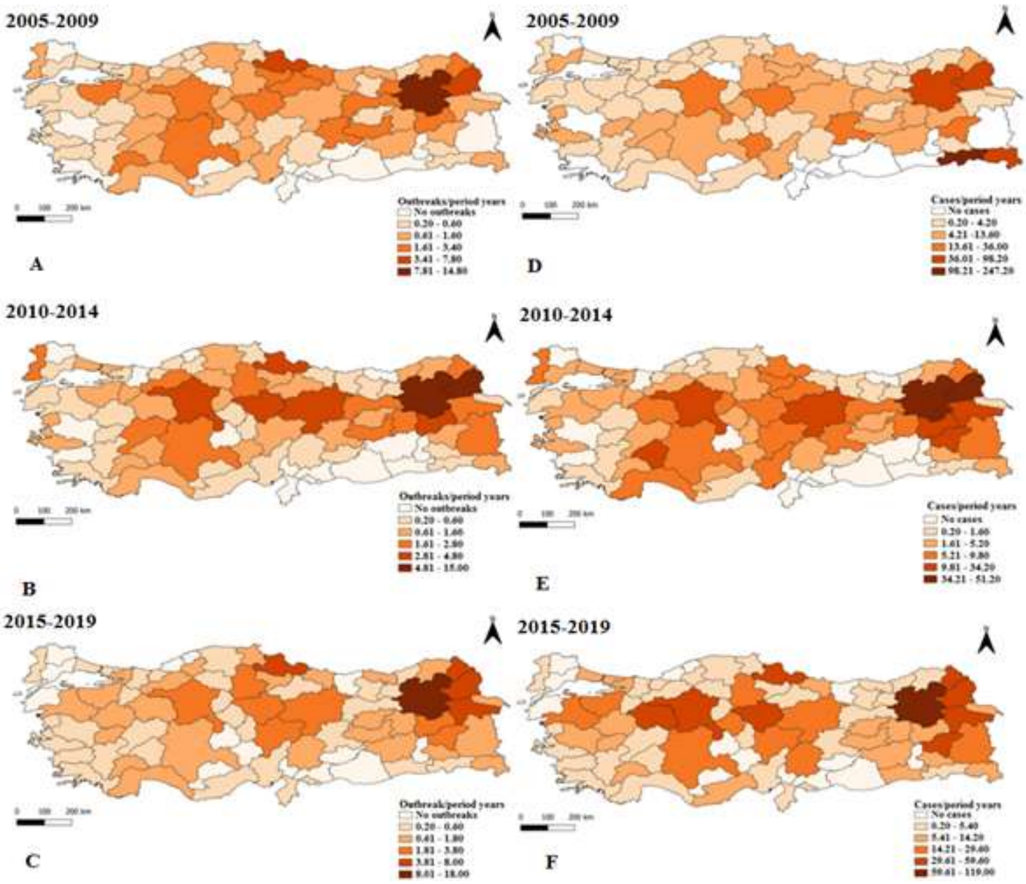

Fig. 2: Mean distribution of anthrax outbreaks in the eighty-one (n=81) provinces of Türkiye at different periods. A) 2005-2009. B) 2010-2014. C) 2015-2019. Mean distribution of anthrax cases in the eighty-one (n=81) provinces of Türkiye at different periods. D) 2005-2009. E) 2010-2014. F) 2015-2019.

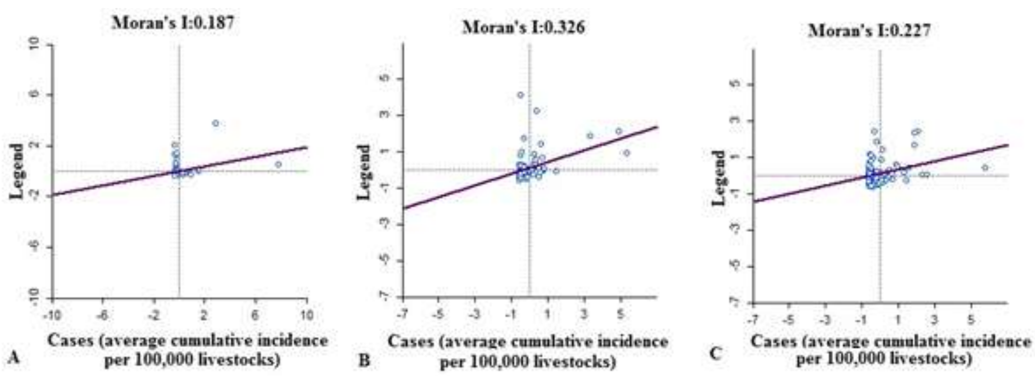

Fig. 3: Moran's *I* scatter chart of the number of anthrax cases. A) 2005-2009, B) 2010–2014, C) 2015-2019.

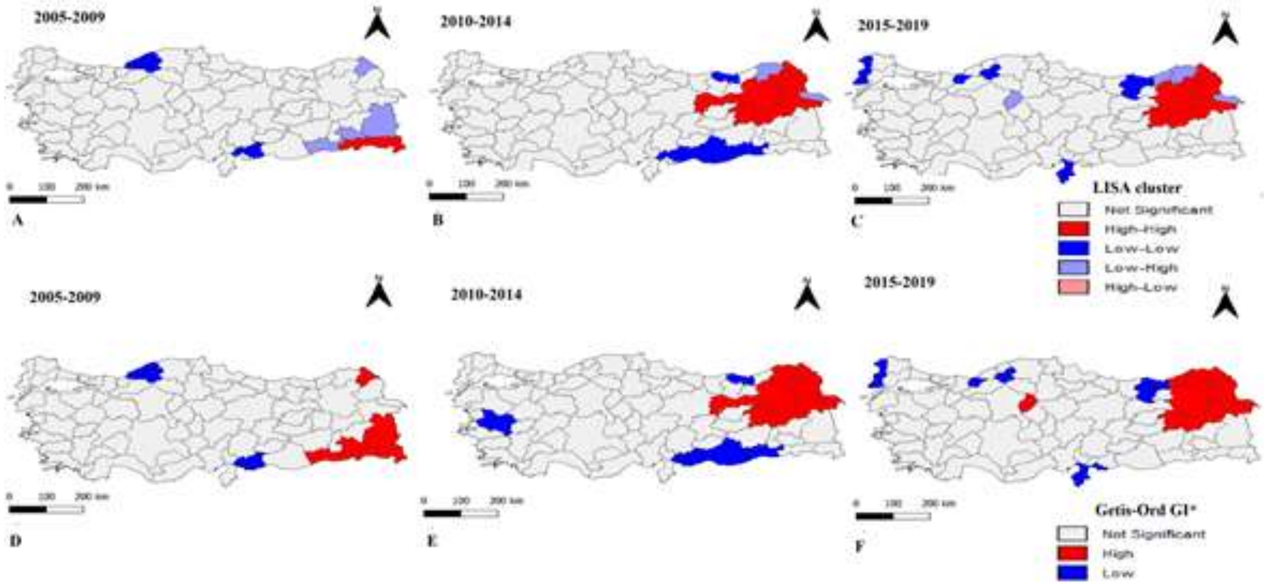

Fig. 4: Identification of anthrax significant clusters with LISA and Getis-Ord GI*.

Table 1: Proportions of anthrax (outbreaks and cases) in Türkiye by year, region, season and species between 2005 and 2019.

	Anthrax Outbreaks		Anthrax Cases		
Variable	Frequency (%)	95%CI	Frequency (%)	95%CI	P-value
Year					
2005	111 (7.19)	(6.02 - 8.48)	1702 (15.92)	(15.26 - 16.64)	P<0.001
2006	100 (6.48)	(5.25 - 7.71)	664 (6.21)	(5.76 - 6.7)	
2007	116 (7.51)	(6.22 - 8.81)	578 (5.41)	(5 - 5.87)	
2008	94 (6.09)	(4.99 - 7.25)	708 (6.62)	(6.18 - 7.1)	
2009	76 (4.92)	(3.89 - 6.09)	377 (3.53)	(3.18 - 3.86)	
2010	82 (5.31)	(4.21 - 6.48)	210 (1.96)	(1.7 - 2.25)	
2011	99 (6.41)	(5.18 - 7.58)	463 (4.33)	(3.94 - 4.71)	
2012	135 (8.74)	(7.38 - 10.17)	591 (5.53)	(5.11 - 5.98)	
2013	121 (7.84)	(6.54 - 9.2)	445 (4.16)	(3.76 - 4.58)	
2014	95 (6.15)	(4.99 - 7.32)	313 (2.93)	(2.63 - 3.27)	
2015	71 (4.6)	(3.63 - 5.7)	284 (2.66)	(2.35 - 2.96)	
2016	73 (4.73)	(3.69 - 5.83)	875 (8.19)	(7.64 - 8.71)	
2017	114 (7.38)	(6.15 - 8.74)	768 (7.19)	(6.66 - 7.67)	
2018	160 (10.36)	(8.87 - 11.85)	1582 (14.8)	(14.15 - 15.49)	
2019	97 (6.28)	(5.05 - 7.51)	1128 (10.55)	(9.96 - 11.15)	
Region					
Aegean	63 (4.08)	(3.11 - 5.12)	406 (3.8)	(3.46 - 4.18)	P<0.001
Black Sea	293 (18.98)	(17.16 - 20.98)	971 (9.08)	(8.56 - 9.61)	
Central Anatolia	270 (17.49)	(15.61 - 19.49)	2211 (20.69)	(19.91 - 21.48)	
Eastern Anatolia	705 (45.66)	(43.13 - 47.93)	4539 (42.47)	(41.53 - 43.44)	
Marmara	108 (6.99)	(5.76 - 8.35)	591 (5.53)	(5.11 - 5.99)	
Mediterranean	76 (4.92)	(3.95 - 6.02)	504 (4.72)	(4.31 - 5.11)	
Southeastern Anatolia	29 (1.88)	(1.23 - 2.59)	1466 (13.72)	(13.08 - 14.36)	
Season					
Autumn	462 (29.92)	(27.91 - 32.25)	3240 (30.31)	(29.44 - 31.19)	P<0.001
Spring	221 (14.31)	(12.63 - 15.93)	863 (8.07)	(7.61 - 8.62)	
Summer	631 (40.87)	(38.41 - 43.26)	4537 (42.45)	(41.53 - 43.34)	
Winter	230 (14.9)	(13.15 - 16.71)	2048 (19.16)	(18.43 - 19.95)	
Species					
Cattle			5314 (49.72)	(48.80 - 50.66)	P<0.001
Sheep			4272 (39.97)	(39.05 - 40.88)	
Goat			1041 (9.74)	(9.18 - 10.33)	
Equidae			59 (0.55)	(0.42 - 0.69)	
Wildlife (species unspecified)			2 (0.02)	(0.00 - 0.05)	

The clusters in 2005-2009, 2010-2014 and 2015-2019 with LISA and Getis-Ord GI*, respectively (Fig. 4). Southeastern and Eastern Anatolia region had high local anthrax clusters in 2005-2009 (Fig. 4A, 4D). But Eastern Anatolia region had significantly high local anthrax clusters in 2010-2014 and in 2015-2019 with both LISA and Getis-Ord GI*. Low–high (few numbers of cases in some provinces with more numbers of cases in surrounding provinces) outliers were determined in 2005-2019 with LISA cluster (Fig 4A, 4B, 4C). Especially significant clusters were detected in Eastern Anatolia region.

Almost half of the outbreaks were detected in the Eastern Anatolia region (45.66%; 705/1544). There was an important relationship between the region and the number of outbreaks. Additionally, there was a significant association between examined years and outbreaks, in 2018 reporting the most anthrax outbreaks (10,36%; 160/1544). Season was related with the number

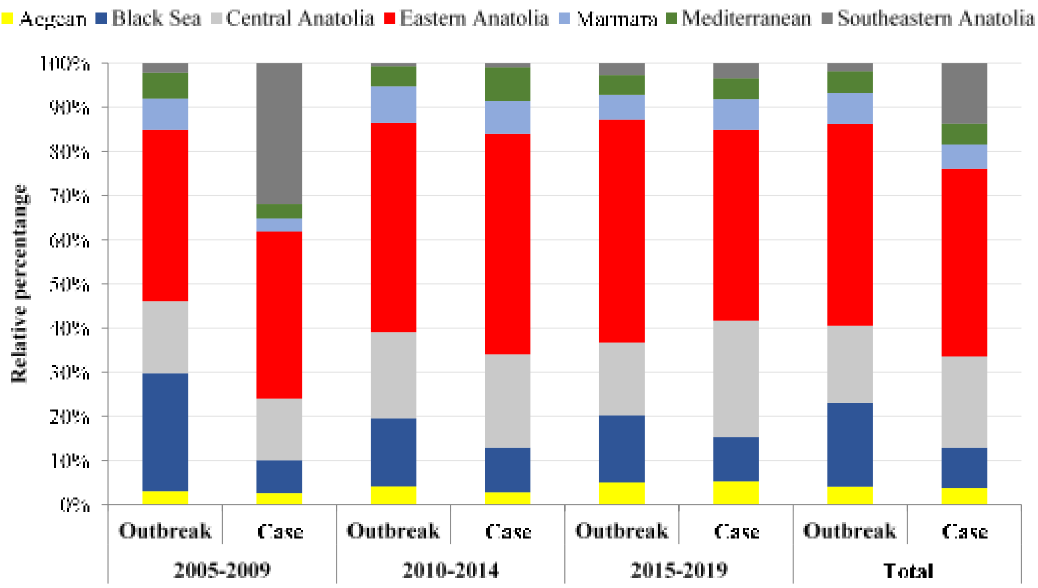

Fig. 5: Region-wise analysis of cumulative anthrax outbreaks and cases in different periods in Türkiye (2005-2019).

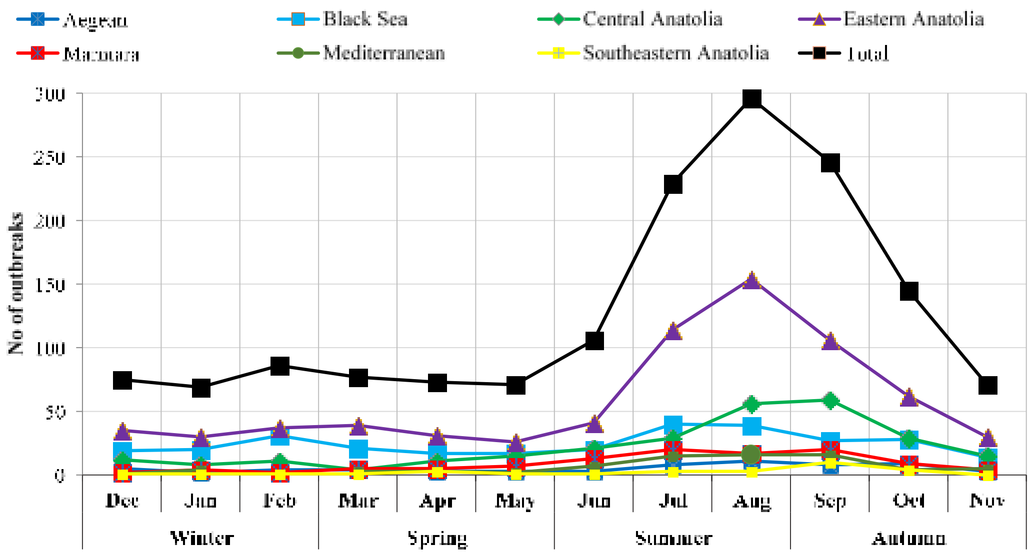

Fig. 6: Month-wise analysis of cumulative anthrax outbreaks in different region in Türkiye (2005–2019).

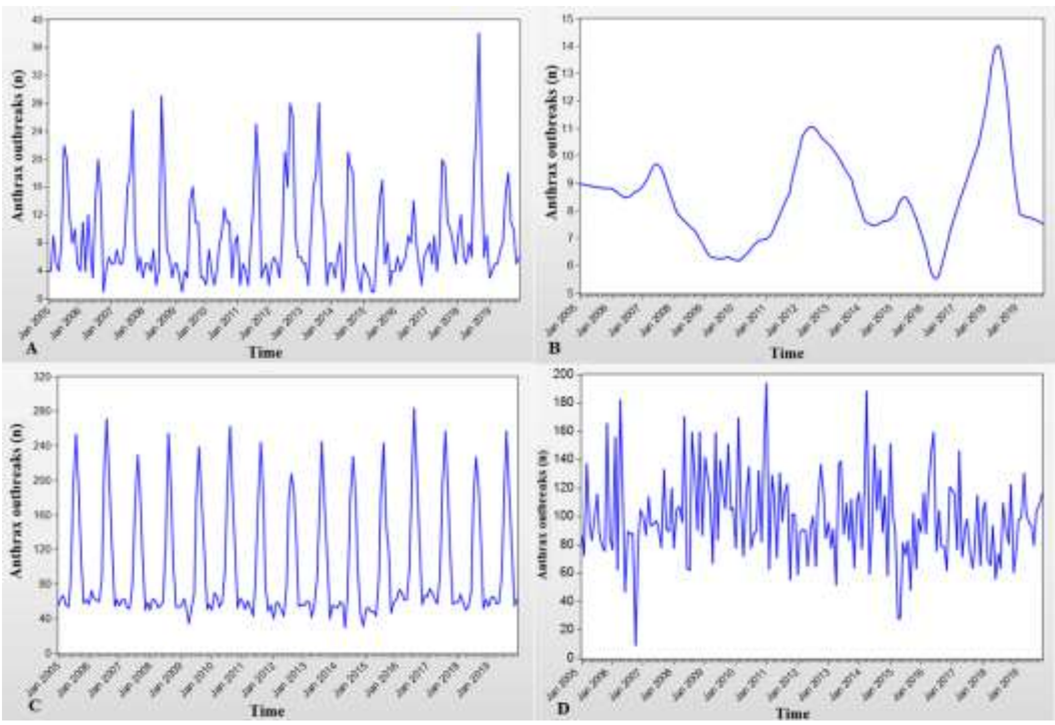

Fig.7: The decomposition with TRAMO/SEATS method of anthrax outbreak series. A) The original time series. B) The trend component. C) The seasonal component. D) The irregular noise component.

of outbreaks (P<0.001), with the summer season reporting the most number of anthrax outbreaks (40.87%; 631/1544) (Table 1).

There was a significant relationship between regions and cases, with the most of cases recorded in Eastern Anatolia (42.47%; 4539/10688) and the fewest (3.80%; 406/10688) in the Aegean region. The most number of cases were recorded in 2005 (15.92%; 1702/10688), was significantly associated with cases. Examined seasons were significantly associated with the number of cases. The cases that were seen over time had a significant relationship with the species of animals, with a significant proportion (49.72%; 5314/10688) of cases reported in cattle (P<0.001) (Table 1). The details of the anthrax outbreaks and cases in different regions in different periods of analysis were presented (Fig. 5).

Temporal pattern of anthrax: Türkiye is situated between the subtropical and mid-latitude temperate climate zone. Country's high, varied geography gives rise to a wide range of climatic conditions. Based on different climatic zones, seasons in Türkiye were described as spring (March to May), summer (June to August), autumn (September to November), and winter (December to February). The most number of outbreaks were calculated in the month of August (n=296), making up 19.17% of total recorded outbreaks and the fewest in January (n = 69), making up 4.47% of total recorded outbreaks (Fig. 6). The monthly distribution of anthrax outbreak from 2005 January to 2019 December was indicated by the time series plot. Three components which are trend component, seasonal and irregular noise component by TRAMO/SEATS method were produced. The outbreak data's trend component revealed a trend with irregular variances and a varying trend. As a result of there was no obvious indication of a trend in the time series and it was discovered that there was a seasonal effect after using the TRAMO/SEATS approach to decompose the outbreak series (Fig. 7).

DISCUSSION

Türkiye has a very important place in terms of transboundary animal diseases because it has a unique geographical location and is adjacent to countries with large naive animal populations. It has a long history of being a high-risk area for outbreak diseases. Unfortunately, there is not much research on Anthrax disease in the prior studies, and none have investigated at the spatial and temporal trends of anthrax in Türkiye. This makes the significance of the findings fairly obvious. The results of this study offer a comprehensive overview of the seasonal and spatiol-temporal dynamics of livestock anthrax in Türkiye from 2005 to 2019.

In this study Moran's I statistics and hotspots for anthrax in Türkiye were explained for the first time using 15 years of passive surveillance information. High-high and low-low clusters, and hotspots were identified. The main objectives of this study are to identify the clusters, seasonal variation of and the spatial pattern of anthrax cases at the province level in Türkiye. As far as I'm aware, this study is the initial study to have ever been conducted in Türkiye that used Moran's I and Gi* statistics to explore spatial patterns.

In this study, Moran's I coefficients were calculated first in order to analyze the relationship between anthrax cases in any province and anthrax cases in neighboring provinces. Spatial autocorrelation indicates whether anthrax numbers are associated with close locations. Accordingly, it was observed that the spatial autocorrelation of anthrax cases is positive across the country. Moran's I values for anthrax were recorded in the range of 0.187–0.326, confirming the presence of spatial structure. Across the country, local disease clusters can be found using local spatial autocorrelation analysis (Anselin, 1995). In this study, the number of high-high clusters increased in the examined periods after the first period. In the first period, high-high clusters were observed in Sirnak bordering Syria and Iraq, and Hakkari bordering Iraq and Iran. The danger of animal disease spreading is increased by sharing borders with Iran, Iraq, Türkiye, and Syria, as well as by wars and conflicts, inadequate precautions, insufficient quarantine applications, and unregulated transport of animals (Jaff, 2016). Later, numerous high-high clusters were observed in the east of the country. High-high clusters were changed places from the Southeastern to the Eastern Anatolia regions. The reason for this may be that immigrants dealing with livestock move to the highlands in the summer and to the pastures in the winter and carry the disease to the east.

The analysis revealed regional and provincial differences in anthrax outbreaks and cases. The majority of outbreaks and cases were found in the Eastern Anatolia region, particularly in the provinces of Erzurum and Kars. The finding is consistent with research examining the Current Situation of Anthrax in Turkey between 2007 and 2019 (Kadanalı *et al.,* 2020). Even though it has significant potential for animal husbandry, the Eastern Anatolia region is one of those with the big structural issues (Diler *et al.*, 2022). The fact that the disease is very common in the Eastern Anatolia region in current study findings may be due to the fact that structural problems still continue. There are international restrictions in place to lessen the hazards because animal migrations play a significant role in the spread of epidemic diseases. Although these restrictions, diseases frequently arise as a result of transfers of animals. When the years 2010-2019 are evaluated, important clusters have been determined in Eastern Anatolia due to the inability to control animal movements, especially from Türkiye's eastern neighbors. In Türkiye, significant animal migrations in Erzurum province in Eastern Anatolia, to significant consuming areas both domestically and abroad result in severe epidemics (Coban *et al.*, 2013; Özlü *et al.*, 2020). The current study's analysis of anthrax data spanning 15 years revealed that the most number of outbreaks and cases found in Erzurum are consistent with this information.

Among the evaluated dates in Türkiye the fewest number of outbreaks and cases were determined in the Southeastern Anatolia region. One of the possible reasons for this may be the insufficient reporting of diseases in some provinces in in the Southeastern Anatolia region (Cakır *et al.,* 2022). But, between 2005 and 2009, outbreak clusters were observed in these areas due to probable animal entry from Türkiye's southern neighbors.

Due to its geographical location, Türkiye is generally within the influence of the Mediterranean climate, which is among the sub-tropical climates. The latitude difference (6°) between north and south also plays an important role in temperature variation. Generally, summers in the country are hot and dry (Baylan and Ustaoglu, 2020). The finding that anthrax outbreaks and case rates are higher in the summer (dry and hot) season is consistent with many studies (Chikerema *et al.,* 2012; Munang'andu *et al.,* 2012; Turner *et al.,* 2013; Gachohi *et al.,* 2019; Kadanalı *et al.,* 2020; Nderitu *et al.,* 2021). Anthrax is a hot-season disease, as has been widely observed, supporting the study's conclusions. Hot and dry weather during anthrax seasons stresses animals and lowers their own biological barrier to disease permitting spores to be infectious at low dosages. Because prolonged exposure to heat can modify the nonspecific local resistance of the skin and mucous membranes, which facilitates the entry of pathogenic organisms, in addition to influencing nutrition, behavior, and management (Hugh-Jones and Blackburn, 2009; Chikerema *et al.,* 2012).

The findings of this study revealed that the most anthrax epidemics and cases were seen in the summer season. This circumstance can be considered as a reflection of the rise in animal migrations occurring concurrently with the rise in transhumance activities during the summer months in Türkiye and the meeting of more vulnerable animals with the pasture (Thevenin, 2011). Because, due to transhumance activities, it has been reported that animals are displaced by trucks or on mountain roads, especially in the Eastern Anatolia region, in summer. In addition, the fact that soil-borne anthrax is observed more frequently in summer and autumn can be considered as a reflection of the fact that the lands create grazing areas for animals following the agricultural harvest in these seasons and that active spores are taken more intensely from these areas. It was reported that soil conditions and predicted hot-dry climatic conditions facilitate the survival of Bacillus anthracis spores and cause subsequent anthrax outbreaks (Driciru *et al.*, 2020).

In this study, higher anthrax outbreaks and cases were seen in cattle compared to other species, this finding was consistent with studies reported in Australia, Kazakhstan, Lesotho, Ukraine and China (Turner *et al*., 1999; Aikembayev *et al.,* 2010; Bezymennyi *et al.,* 2014; Chen *et al.,* 2016; Lepheana *et al.,* 2018). It has been stated that while cattle graze, they swallow a lot of soil by pulling the plant from the soil, while goats generally only wander in the grass, which leaves them lower exposed to spores in the soil (Hugh-Jones and Blackburn, 2009). Cattle are likely to be more sensitive to anthrax, either because they may consume higher doses of the virus due to their feeding niche, or because insects and biting flies can technically spread Bacillus anthracis to them (Chen *et al.,* 2016). Consequently, it is possible that changes in population distribution, dietary preferences, and types of agricultural systems are responsible for the diversity in the affected species. The finding that cattle are more affected than other animals is significant, as it suggests that implementing a specific anthrax control program that only includes routine immunization of cattle may be more economically efficient and practical.

In this study, anthrax cases recorded over a fifteen-year period totaled 10688. This is significantly more than the 2261 cases recorded in China during an eight years, the 851 cases recorded in Ghana during eleven years, the 526 cases reported in Lesotho during eleven years (Chen *et al.,* 2016; Kracalik *et al.,* 2017; Lepheana *et al.,* 2018). As a result, anthrax is endemic in Türkiye. The outbreak data's trend component revealed a trend with irregular variances and a varying trend. There was no obvious indication of a trend in the outbreak series and there was discovered a seasonal effect once the outbreak series decomposed using the TRAMO/SEATS approach. In many studies, the effect of the season on anthrax has been expressed in consistence with this study (Munang'andu *et al.,* 2012; Lepheana *et al.,* 2018; Nderitu *et al.,* 2021; Zorigt *et al.*, 2021).

This study has limitations because it lacks any control over the accuracy of the data collected, a problem that naturally arises in retrospective research. Therefore, a number of actions can be made to enhance the quality of data collecting for upcoming research. In addition, awareness and training of animal owners, training of animal health workers, detection and mapping of contaminated pastures, preparation of decontamination programs and continuity of vaccination studies should be ensured.

Conclusions: In this study, seasonal and spatio-temporal patterns of livestock anthrax were evaluated. It was determined that anthrax outbreaks and cases were seen more intensely in the summer season in Türkiye and the risk of disease was higher in the Eastern Anatolia region. It was concluded that those living in these regions may have a higher risk of contracting anthrax. Therefore, considering the study findings, it is thought that it is important to concentrate control and vaccination strategies, especially in this region, where disease outbreaks tend to occur. Considering the limitations of this study, more investigation is needed to describe the causative agents of anthrax outbreaks, especially in the Eastern Anatolia region. Also, the findings of this study are very important as they can be of great benefit to policy makers and national veterinary services in formulating a policy for the prevention and control of anthrax in Turkiye.

Authors contribution: Tuba Bayir designed the study, collected the data, performed the analysis and wrote the manuscript.

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