Veterinary Integrative Sciences 2023; 21(2): 411 - 427 DOI; 10.12982/VIS.2023.029

Vet Integr Sci

Veterinary Integrative Sciences

ISSN; 2629-9968 (online)

Website; www.vet.cmu.ac.th/cmvj

Research article

Temporal trend and high-risk areas of rabies occurrences in animals in Nepal from 2005 to 2018

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Abstract

Rabies is an important zoonosis in both the public and animal health domains. The occurrences of animal rabies have been continuously reported in Nepal. For the effective control and management of animal rabies, a better understanding of rabies epidemiology is essential. Therefore, the objectives of this study were to determine the spatial distribution and to describe the epidemiological characteristics of animal rabies occurrences in Nepal. Official reports of rabies occurrences from 2005 to 2018 were analyzed using the Global Moran's Index and Local Moran's Index. The study revealed an increasing trend in the later years of the study period after 2014 with occurrences clustered around the southern region of the country. For the overall period, the high—high clustering areas were mostly found in Dailekh and Kailali. In addition, different areas were visualized as high-risk areas in various years. This study identified the high-risk areas of rabies; thus, authorities and stakeholders can utilize this finding in enhancing the rabies control program in the country.

Keywords: Epidemiology, Nepal, Rabies, Spatial clusters, Trend

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Article history; *received manuscript: 13 January 2023,*
revised manuscript: 8 February 2023,
accepted manuscript: 22 February 2023,
published online: 13 March 2023
Academic editor; *Korakot Nganvongpanit*

INTRODUCTION

Rabies is one of the oldest known diseases, reported for over 4000 years, with the highest case fatality rate of any conventional etiologic agent. Several similar viruses in the Lyssavirus can lead to rabies, of which the rabies virus (RABV) is the most extensively disseminated (Grover et al., 2018). While all warm-blooded animals appear susceptible to RABV including humans and livestock, dogs have been considered as the major source of infection. Dog bites cause 95% of human rabies cases but the figure rises to 99% in endemic regions (Ma et al., 2020). However, a small percentage of human rabies also results from wild populations such as foxes, wolves, jackals, mongoose, raccoons, skunks, and bats. This occurs mostly in affluent countries that have successfully suppressed domestic rabies occurrences (El-Neweshy et al., 2020; Riccardi et al., 2021). Approximately 59,000 people are reported to die of rabies annually in over 150 countries, with more than 95% of cases occurring in Asian and African regions. This results in a substantial increase in the health and economic burden in these parts of the world. (Taylor and Nel, 2015; Riccardi et al., 2021).

Nepal is a landlocked country surrounded by India in the east, west, and south and China in the north. Nepal shares an open border with India in the south, the country with the heaviest rabies burden, accounting for 35% of human deaths globally (Epidemiology and burden of disease, 2022); whereas, China is the second country after India in the annual incidence of human rabies cases (Guo et al., 2013). In Nepal, animal rabies has been an endemic and notifiable disease since 1995; however, human rabies is still not a notifiable disease (Pal et al., 2021). Urban areas are the predominant source of human rabies, with more than 96% of rabies patients reported during 1991-2000 showing a history of rabid dog exposure (Gongal and Wright, 2011). According to the reports from the Veterinary Epidemiology Section and Department of Health Services in Nepal, rabies cases in animals are on the rise, while rabies-related human mortality has fluctuated in recent years (Annual Report, 2018; Quarterly Animal Health E-Bulletin, 2018).

The present rabies control programs generally focus on urban and developed areas, but the rural and less developed areas contribute to a significant number of animal bites and rabies cases in Nepal. Moreover, there are well-facilitated laboratories only in major cities resulting in inadequate reporting and ineffective surveillance of rabies in rural areas. (Pantha et al., 2020). The best and most sustainable pathway to control and eliminate rabies appears to be the One Health model, and this requires the exchange of information and data among all parties and across all disciplines within the country (Acharya et al., 2020; Kiratitana-olan et al., 2022). Veterinarians and/or public health officials can facilitate action by accessing the information on the spread of cases in space and time. Consequently, spatial and temporal analysis are methods for specifying geographical areas and periods of time.

Spatial analysis is commonly used for disease cluster detection in veterinary science (Carpenter, 2001; Robertson and Nelson, 2010). Generally, the purpose of spatial analysis in animal and public health is to describe existing spatial patterns, to understand the biological mechanisms that lead to the occurrence of disease, and to predict what will happen in the medium- to long-term future or in different geographical areas (Stevens and Pfeiffer, 2011). Understanding the spatial distribution of rabies in animals and humans, as well as its transmission mechanisms, is crucial for projecting the disease's onset, spread into new geographic areas, and guiding targeted interventions (Guo et al., 2013). Studies of the spatial and temporal patterns of rabies in humans and animals have allowed researchers to pinpoint places and times where animal-to-human transmission is most prevalent (Guo et al., 2013; Grover et al., 2018; Santos et al., 2019; Bouslama et al., 2020; Kalthoum et al., 2021). For instance, Gibson et al. presented the elimination of human rabies in the state of Goa, India, through an integrated 'One Health Approach' (Gibson et al., 2022). However, the study essentially relied on spatial and temporal data to identify clusters of canine-mediated rabies.

Few studies have been published in Nepal on rabies and its epidemiology (Devleesschauwer et al., 2016; Karki and Thakuri, 2010), but none aimed to analyze the spatial distribution and temporal pattern of the disease. However, for the effective management and surveillance of rabies, a better understanding of disease epidemiology including spatial and cluster analysis is essential. Thus, our study aimed (i) to analyze and describe the epidemiological pattern of animal rabies occurrences from 2005 to 2018 and (ii) to detect the potential spatial clusters of animal rabies in different districts of Nepal. The findings will help to understand the epidemiology of animal rabies in terms of geography and develop rabies control programs specific to the area under consideration.

MATERIALS AND METHODS

Data Collection and Management

For this study, retrospective animal rabies data from the period of 2005 to 2018, were retrieved from the Veterinary Epidemiology Section (VES) and Central Veterinary Laboratory (CVL) of Nepal. The datasets from VES were the cumulative data of monthly epidemiological reports of the District Livestock Service Offices (DLSO). There are 999 Livestock Service Centers (LSC) strategically located in Village Development Communities (VDCs) and municipalities, which are the lowest administrative level in Nepal. Animal health and disease data were acquired from the LSCs and were reported to VES by DLSO as animal disease epidemiological reports in a specified format. If there was an occurrence of one or more animals with clinical signs of rabies in a particular time and area, the event was recorded by the officials. The suspected case of animal rabies was defined by district veterinary officers based on the signs and the confirmation of animal rabies cases was made by Fluorescence Antibody Test (FAT) in CVL.

The datasets from VES were compiled and categorized based on the reported date, district of the outbreak, and number of occurrences for spatial distribution, while for descriptive statistics, it was grouped for month, year, and season. In addition, species of animal rabies occurrences from 2013 to 2017 were arranged for further analysis from the data available from CVL.

Microsoft Excel 2013 was used for entering and categorizing data. After cleaning, the collected data were verified and validated by the authorized organization. Geographical data were accessed from the National Spatial Data Infrastructure (NSDI) Clearing House/Data Center provided by the Survey Department, Nepal. Since veterinary services were present in every one of the 75 districts for epidemiological surveillance, districts were chosen as the smallest unit for spatial analysis.

Data Analysis

Descriptive Analysis

Descriptive data analyses were performed to describe the annual, monthly, and seasonal trends of animal rabies occurrences. A local polynomial regression fitting method was used to create a trendline since the occurrences appeared to show a non-linear pattern. Also, monthly bar graphs for individual years were created to evaluate the occurrence of animal rabies across a year. Seasonal distribution of rabies occurrences was assessed by aggregating the cases of occurrences into the four seasons of the year. The seasons were classified as per the guidelines of the reporting format of the Veterinary Epidemiology Section:- summer (June, July, August), autumn (September, October, November), winter (December, January, February), and spring (March, April, May). In addition, stacked bar graphs were used to visualize the species distribution data from CVL. All the descriptive analyses were performed using software R studio-2022.07.01-554 and presented as trend lines and bar graphs.

Seasonality Test

A time series of monthly rabies occurrences were statistically tested to determine whether it has a seasonal pattern using Ollech-Webel seasonality test in "seastests" package with R (Ollech and Webel, 2020).

Spatial Analysis

In this study, the reported occurrence cases of animal rabies from the study period were aggregated, and a choropleth map was created to estimate the burden of animal rabies in every district of Nepal while mapping was conducted for individual years as well to understand the variation of rabies occurrence in the same district in different years. A choropleth map provides a visualization of geographical areas divided with different colors or shades to present spatial variation of a quantity such as population and disease incidence at a glance. QGIS version 3.22.11 was used for creating maps.

Spatial autocorrelation analysis including global autocorrelation and local autocorrelation was performed. First, the global Moran's I was used to test the spatial correlation of the whole study area. Further, the local Moran's I was utilized to determine the spatial autocorrelation of each spatial unit and its neighboring unit. These analyses were performed using the software GeoDa.

First, contiguity-based spatial weight was constructed for each district by creating a first-order queen contiguity weight file to define the spatial relationships using the rabies occurrences as the variable of interest. Global Moran's I is simply a correlation coefficient to measure how one object is similar to others surrounding it (Anselin, 2020a). This index provides the information whether the pattern of rabies occurrences in Nepal are clustered or dispersed or random. In the study, the index measures rabies occurrence in particular districts and how it is related to other districts. The formula for the global Moran's I is as follow;

$$I = \frac{N \sum_i \sum_j (x(s_i - \bar{x})(x_j - \bar{x})}{\sum_{ij} w_{ij} \sum_i (x_i - \bar{x})^2}$$

where s indicates location and i, j specify spatial units; w_{ij} denotes the spatial connectivity matrix; x_i is the value of the attribute in the i geographic unit; $\bar{x}$ is the mean value of the study area and N is the total number of geographic units.

A value of Moran's I of 0 implies that rabies occurrences are perfectly random in space. A Moran's I value of +1 indicates perfect clustering, whilst a value of -1 is indicative of perfect dispersion. The statistical significance of Moran's I was assessed using Z-statistics by conducting Monte Carlo randomization with 999 permutations. The spatial correlation at the global level is significant($p < 0.05$) when the Z-score is greater than 1 or less than -1. (Kumar Pant et al., 2017).

When the global spatial autocorrelation was significant, a local indicator of spatial association (LISA) test was used to further identify local spatial autocorrelation as global Moran's I does not provide an indication of the location of the clusters. One of the most used LISA is the local Moran's I. The basic idea behind local Moran is that it looks at the value of a given variable (rabies occurrence) in a specific location (district) and if it has high value along with its neighbors, the location is said to have hot spot and inversely cold spot when value is low. Thus, based on the LISA, districts in Nepal can be classified into different risk areas. The formula for the local Moran's I is as follow;

$$I_i = ((x_i - \bar{x}))/m_2) * (\sum w_{ij} * Zj)$$

where w_{ij} are the weight and z_j refers to $x_i - \bar{x}$,. The term x is the value of the variable at location i and $\bar{x}$ indicates the mean values of the variable in the formula. The term m_2 refers to $\sum(x_i - \bar{x})^2/n$, where n is the number of observations. (Anselin, 2020b).

The indication of significance from the Local Moran's I when combined with the location of each observation in the Moran scatterplot allows for the classification of significant locations as high—high and low—low spatial clusters and high—low and low—high spatial outliers. High—high means districts/regions with high occurrences of rabies are surrounded by neighboring districts/regions with high occurrences of rabies with a significant spatial cluster of high rabies occurrences. Low—low indicates a spatial cluster of low rabies occurrences surrounded by neighboring districts/regions with low rabies occurrences. Finally, the significance and clustering were visualized in the form of a LISA cluster map while the high–high clustering districts across the study period were tabulated. The geographical information system software QGIS version 3.22.11 was used to create LISA cluster maps for the years from 2005 to 2018 after corresponding analyses were conducted in GeoDa.

RESULTS

Descriptive Analysis

From the time period of 2005 to 2018, there was a total of 1085 animal rabies occurrences reported. The trend was high in the initial years (2005-2007) with cases declining in the following years. There seemed to be relatively steady occurrences from 2010 to 2013 with an average of 54 occurrences reported in this period. The number has risen lately and reached the highest number of occurrences (159) in 2018 as shown in Figure 1. Animal rabies cases in Nepal occurred throughout the year as seen in the monthly bar graph in Figure 2. Figure 2 shows monthly distribution of rabies occurrence for each year which demonstrates that there was no seasonal pattern when the monthly data were tested. This finding was confirmed by the Ollech-Webel seasonality test (p>0.05).

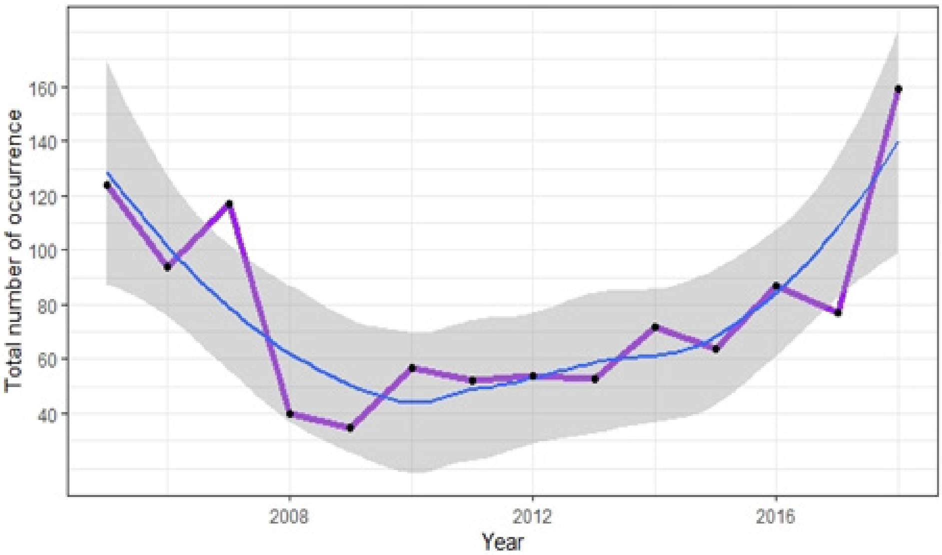

Figure 1 Yearly distribution of animal rabies cases in Nepal from 2005 to 2018 with a non-linear trendline (purple line) and its 95% Confidence Interval based on the local polynomial regression method (blue line).

Figure 2 Monthly distribution of animal rabies cases in Nepal from 2005 to 2018 with distribution shown for every year individually.

Table 1 aggregating the seasonal occurrence revealed that animal rabies occurrences were similar throughout the seasons. Data showed an average of 19 cases recorded on average. In addition, from the records from 2013 to 2017, we found dogs as the species with the greatest number of occurrences (137) followed by cattle (83) and buffalo (74). The cases of rabies were also seen in feline, equine, goat, jackal, pig, and yak as shown in Figure 3.

Table 1 Summarization of average animal rabies cases in Nepal from 2005 to 2018 with standard deviation calculated for every season.

Seasons	Average animal rabies cases in each season (Mean ± standard deviation)
Summer	21.07 ±10.96
Autumn	18.29 ±13.11
Winter	20.29 ±9.91
Spring	17.86 ±10.28

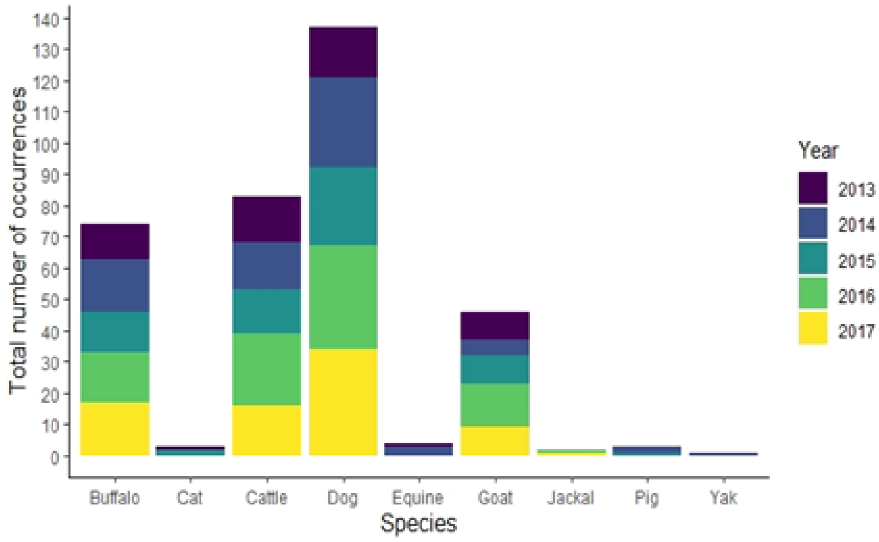

Figure 3 Species-wise distribution of animal rabies cases in Nepal from 2013 to 2017.

Spatial Distribution Analysis

For the spatial distribution analysis, choropleth maps showing the variation in the number of animal rabies occurrence reports were generated for overall time period from 2005 to 2018 (as shown in Figure 4) and for each year individually (in Figure 5 panels A-N). These maps showed a pattern of occurrences towards the southern plains of Terai of Nepal as compared to the other regions. The occurrences were reported from 68 districts throughout the study period with the highest event of occurrences from Siraha (95) followed by Kanchanpur and Surkhet (53 each). The highest number of occurrences in a single year was seen in Taplejung in 2005 (38). Bhaktapur, Darchula, Dolpa, Mustang, Myagdi, Sankhuwasabha, and Solukhumbu were the seven districts without any rabies cases reported in our study frame. In recent years, Siraha had the highest number of occurrences in consecutive years from 2016 to 2018 (Figure 5 panels L-N).

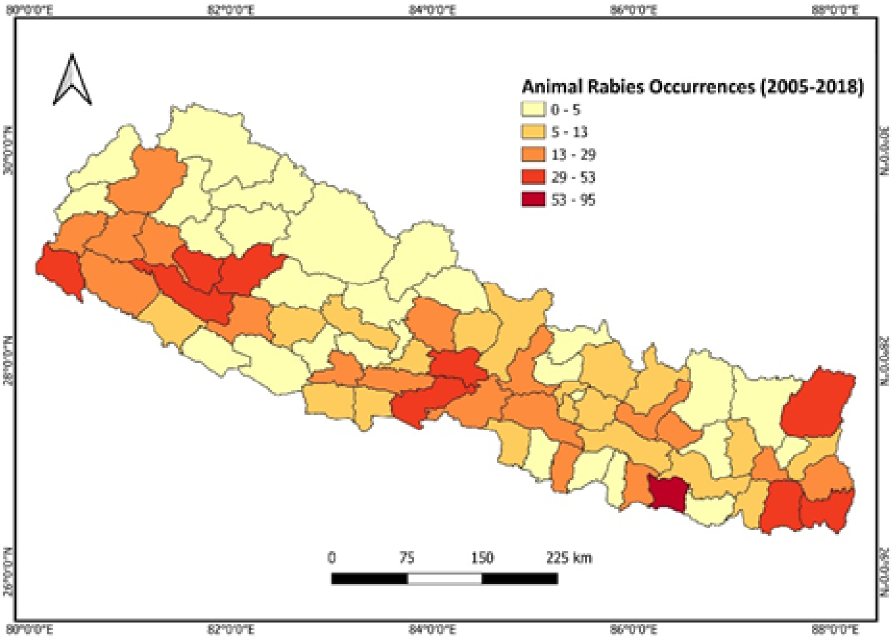

Figure 4 Choropleth map of animal rabies occurrences reported from 2005 to 2018 data for Nepal across all districts.

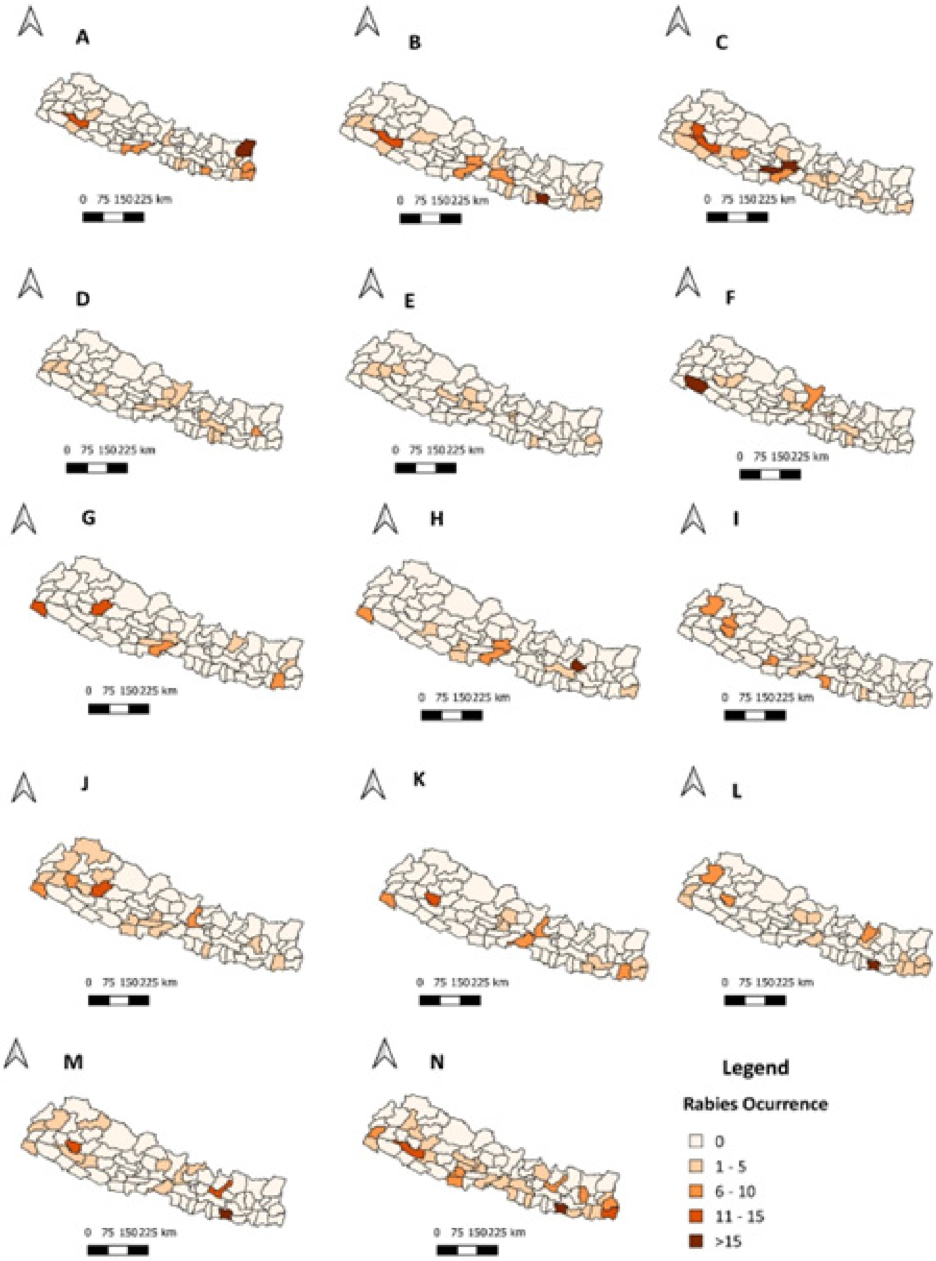

Figure 5 Panels A-N: Number of animal rabies occurrences reported in Nepal for different years from 2005 to 2018 at the district level arranged respectively in panels.

Spatial Autocorrelation Analysis

To explore the spatial dependence of the correlation between occurrences of different districts, Global Moran's I was calculated. The Global Moran's spatial autocorrelation between animal rabies occurrence estimates was significant (Moran's Index = 0.157, p = 0.011, Z score = 2.4883) as shown in the scatterplot (Figure 6). The results indicate the clustering of rabies occurrences with similarities in animal rabies events of adjacent districts with a significant p-value and Z- score greater than 1. Although the results from Global Moran's I indicated significance between the clusters, it does not specify the location of clusters. Hence, the spatial distribution of rabies occurrences at the district level was further investigated for clustering and outliers using the Local Moran's I test. The analysis indicated a high—high clustering of animal rabies incidence in Kailali (p = 0.038) and Dailekh (p = 0.048), while low—low clustering was seen in Mugu (p = 0.013), Mustang (p = 0.02) and Baglung (p = 0.026) for the overall time period from 2005 to 2018 (Figure 7. Panel O). The LISA cluster map was created for every year which identified sixteen high—high clustering districts in different years of the study period as indicated in Table 2.

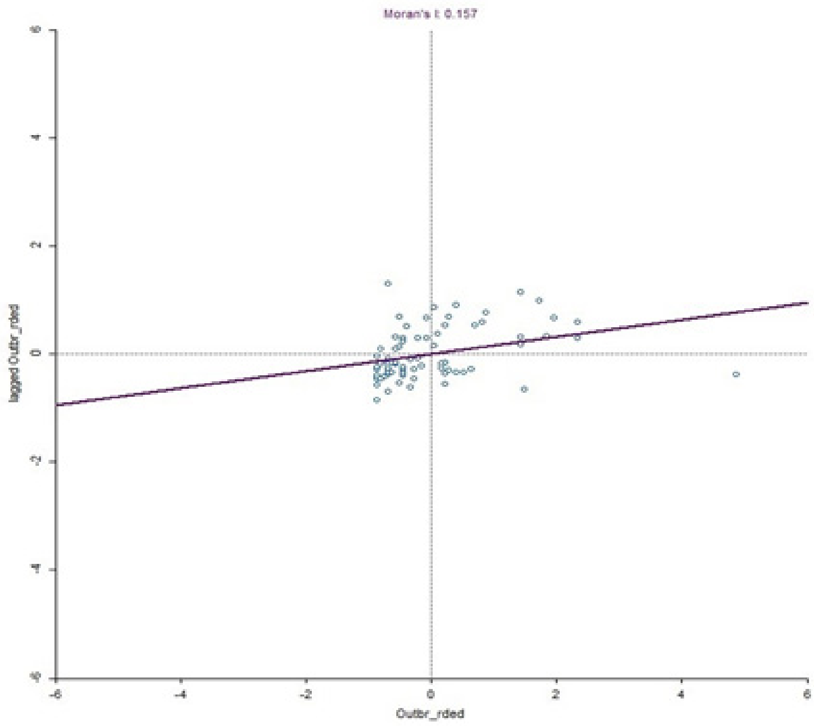

Figure 6 Global Moran's I scatterplot for animal rabies occurrences reported from 2005 to 2018 calculated using GeoDa.

Table 2 Summarization of the statistically significant ($p<0.05$) high—high cluster of animal rabies data at the district level in different years.

Year	Districts	Local Moran's p value
2005	Terhathum	0.033
2007	Doti	0.044
	Tanahun	0.014
	Nawalparasi	0.004
	Palpa	0.042
2009	Kaski	0.035
	Syangja	0.024
2013	Achham	0.022
	Dailekh	0.032
2014	Jumla	0.038
	Kalikot	0.004
	Dailekh	0.004
2015	Ilam	0.049
	Jhapa	0.007
2016	Jhapa	0.042
2018	Saptari	0.029

DISCUSSION

Despite several decades of attempts to eradicate rabies, the disease still exists in Nepal, and one of the major reasons is the lack of proper analysis of epidemiological data related to rabies. This study highlights an increasing trend of the occurrences in the later years of the study period with no marked seasonal pattern and a heterogenous spatial distribution with a geographical pattern and clustering for animal rabies occurrences in specific areas of Nepal. The results from this study reveal that over the 14-year study period, 1085 rabies occurrences were reported with an average of 78 cases per year with no clear increasing or decreasing trend in the apparent incidence of rabies occurrences. Similar erratic trends were seen discussed by Gongal (Gongal, 2006), Karki and Thakur (Karki and Thakuri, 2010), Devleesschauwer et al. (Devleesschauwer et al., 2016), and Pantha et al. (Pantha et al., 2020) for different time periods. The previous studies of Karki and Thakur (Karki and Thakuri, 2010) and Yadav (Yadav, 2012) in Nepal, found the maximum number of rabies cases in the month of February citing the apparent seasonality as the result of an incubation period of animal bites. Our study found the highest number of occurrences in the month of January (Figure 2) but the monthly bar graph (Figure 2) showed a similar number of occurrences across the years and was confirmed by the seasonality test. The seasonality of rabies was demonstrated in several neighboring and South Asian countries as in China (Guo et al., 2018; Subedi et al., 2022) and Bhutan (Tenzin et al., 2011). Although different regions presented different temporal patterns in our study, several other published reports have confirmed the notion of a temporal effect in association with the occurrences of rabies occurrences (Abedi et al., 2019; Baker et al., 2019). As the study suggests that the rabies occurrences reached the peak at the beginning of the year, we suggest that the period around the end of the year would be an appropriate time for implementing vaccination programs.

Initially, Gongal and Rai reported homogenous distribution of rabies occurrences in Nepal (Gongal et al., 2001) but our study presented cases clustered in the districts of southern plains of Terai as seen in the choropleth map (Figures 5 and 6). This might be due to open land border with India allowing stray dog population free access to roam and settlements around the national parks in the districts of Terai. Rabies is endemic in India with 35% of the world's rabies deaths and annual incidence of 1.75 million dog bites as reported in 2018 (India sees 1.75 million dog bites every year, yet we face up to 80% shortage of anti-rabies vaccines, 2018; Radhakrishnan et al., 2020). Movement patterns of free-roaming dogs are irregular and mostly based on the availability of resources (food and shelter) and geographical features (river or land) (Raynor et al., 2020). However, rabid dogs sometimes exhibit erratic behavior with some records of dogs moving more than 15 km from home (Townsend et al., 2013). According to previous studies, rabies virus has been found to spread over distances, from 30 to 50 km/ year in countries of North Africa such as Algeria and Morocco through carrier animals (Talbi et al., 2010; Bouslama et al., 2020). Given the transboundary nature of rabies (Polupan et al., 2019) and with open border to India, there can be increase in the number of carrier animals like dogs and eventually increase in the number of animal rabies occurrences in the southern regions of Nepal. Furthermore, Terai is home to different protected areas, including national parks, wildlife reserves, and conservation areas (Shrestha et al., 2010). There have been fewer sylvatic cases of rabies reported in Nepal since proper surveillance systems for wildlife have not been yet set up. However, we cannot neglect the fact that the protected areas can also be risk factors for occurrences of rabies with significant settlements of people and their livestock around these protected areas and buffer zones (Baral and Heinen, 2007; Allendorf, 2010).

The main focus of this study was to investigate the rabies clustering because the findings would facilitate the identification of potential problem regions that may require special attention when planning rabies prevention and control programs. Based on the global and local spatial autocorrelation analysis, we found that the spatial distribution of animal rabies occurrences presented significant clustering patterns in different years (Figure 7). The study conducted in Tunisia for animal rabies (Kalthoum et al., 2021), in Sri Lanka for canine-mediated rabies (Janrabelge, 2019), and in Brazil for cattle rabies (Santos et al., 2019) also reported significant clusters for rabies cases. LISA cluster maps found the High – High clustering at sixteen districts in various years. Despite the choropleth map showing overall clustering in the south, the High – High clustering districts have varied in terms of location. In the spatiotemporal study of canine rabies in Tunisia (Bouslama et al., 2020), spatial distribution was not fixed through time as in our study. Hence, there might be a shift in cluster locations in the future as well. As we look closely into the districts with the High – High clusters (Table 2), we can see Dailekh (2013 and 2014) and Jhapa (2015 and 2016) featured in consecutive years that may be attributed to a slow response by officials to the outbreaks. An annual vaccination campaign and stabilizing the number of free-roaming dogs are common strategies carried out in rabies endemic countries across the globe (Thanapongtharm et al., 2021). However, the pulse vaccination strategy, in which animals identified in the risk locations are repeatedly vaccinated, should be introduced into these endemic areas of high risk.

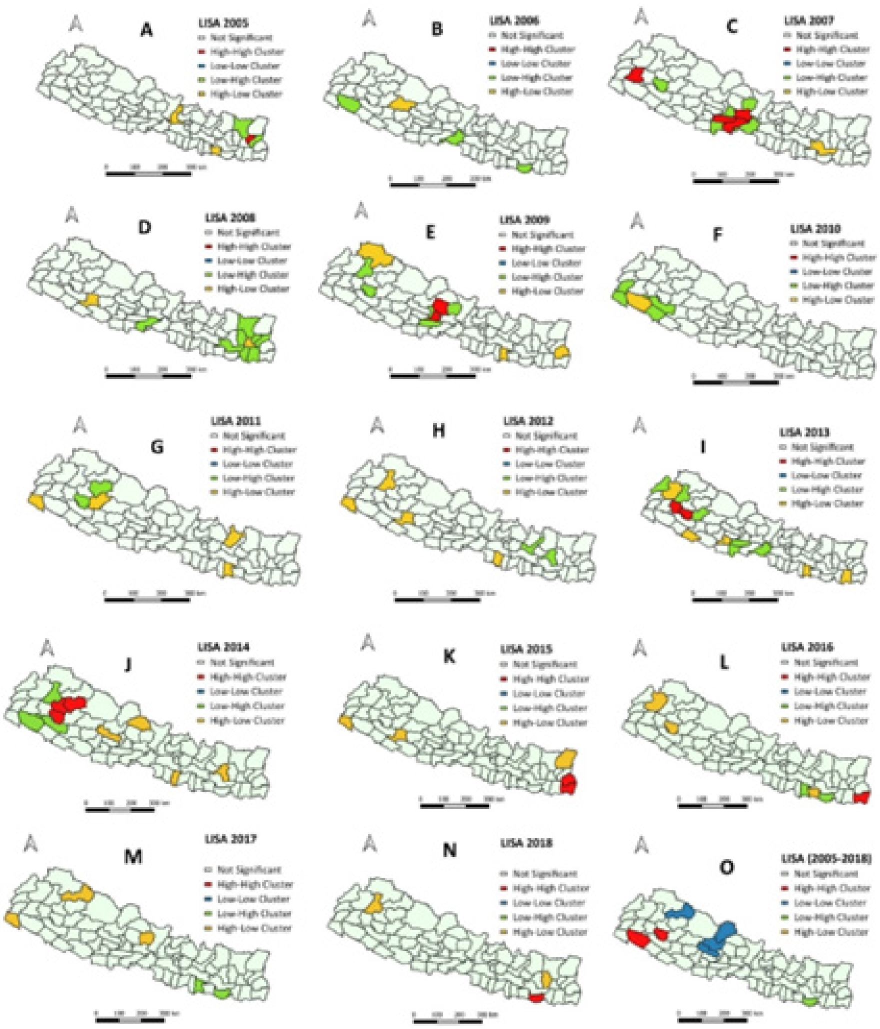

Figure 7 Panels A-O: Map showing the Local Indicator of Spatial Autocorrelation (LISA) cluster of animal rabies occurrences in Nepal from 2005 to 2018.

The epidemiological situation of the disease is comparable to that of many other countries in South and South East Asia (India, Pakistan, Afghanistan, Bangladesh, Myanmar, Indonesia, Sri Lanka, and Thailand) (Gongal and Wright, 2011). Animal rabies is endemic and commonly reported in Nepal with reports from 68 out of 75 districts. Previously, Karki and Thakur had reported cases from 72 districts (Karki and Thakuri, 2010), and this small decrease in the number of districts with occurrences maybe due to rise in awareness about rabies among the general public (Pal, Yawongsa, Bhusal, et al., 2021) and anti-rabies vaccination campaigns for the dog population led by different governmental and private entities on a regular basis across the nation (Acharya et al., 2019).

The results of this study should be interpreted in light of the study's limitations. Firstly, the analysis included reported data collected at district levels and was therefore subject to reporting biases and underreporting. Also, some important data such as number of estimated dog population and number of humans bitten by dogs are not available; therefore, the association between rabies cases and these variables could not be assessed by this study. Secondly, the cumulative passive surveillance data were obtained from the district and could only be used as centroid data for spatial analyses while using point data could have improved the results. The improvement of robust routine data collection is required for better analysis and prediction in future studies. It is worthwhile to note that although the present study has some limitations, our findings of the distribution of the disease and high -risk areas will be beneficial for all the stakeholders working with rabies in Nepal.

We recommend incorporating the spatial and temporal analysis demonstrated herein into further research and surveillance system with additional parameters (history, sex, and vaccination status) of the animals to correlate the underlying risk factors for the outbreak. Similar studies should be conducted for a human rabies dataset that could guide more intervention strategies as a multisectoral and cost-effective approach. The authorities should also increase surveillance and data reporting from all the districts with added parameters about animals. The potential to control rabies relies on epidemiological information, identification of the associated risk factors, socio-economic implications, and an understanding of the disease dynamics. Thus, conducting this research provided much needed epidemiological facts and figures for the rabies occurrences. Hence, the study could be a tipping point for the people working on integrated and multisectoral rabies control and management strategies.

CONCLUSIONS

In summary, animal rabies occurrences have been increasing lately with clusters in the southern regions of the country. The LISA cluster maps showed high—high regions of occurrences in Dailekh and Kailali. With the 'Zero by 30' worldwide call for action to eliminate human rabies deaths by 2030 on the horizon, scientifically driven policies must be rigorously implemented to achieve this goal. This spatial analysis will facilitate and help in the utilization of resources, while designing rabies elimination strategies for countries such as Nepal, which are far from achieving this goal.

ACKNOWLEDGEMENTS

The authors would like to acknowledge the Veterinary Epidemiology Section and the Central Veterinary Laboratory under the Department of Livestock Services for providing animal rabies outbreak data to use in this study. Also, the author would like to extend their gratitude to VPHCAP (Veterinary Public Health and Food Safety Centre for Asia Pacific), Faculty of Veterinary Medicine, Chiang Mai University, under the CMU Presidential Scholarship for all the support.

AUTHOR CONTRIBUTIONS

Swochhal Prakash Shrestha: Conceptualization, Methodology, Software, Data Curation, Formal Analysis, Original Draft Preparation, Visualization
Warangkhana Chaisowwong: Conceptualization, Methodology, Resources, Review and Editing, Supervision, Project Administration
Orapun Arjkumpa: Methodology, Software, Formal Analysis, Review and Editing, Visualization
Mukul Upadhyaya: Data Curation, Validation
Pragya Koirala: Data Curation, Validation
Manju Maharjan: Data Curation, Validation
Swoyam Prakash Shrestha: Data Curation, Validation, Review and Editing
Veerasak Punyapornwithaya: Conceptualization, Methodology, Software, Formal Analysis, Resources, Original Draft Preparation, Review and Editing, Visualization, Supervision, Funding Acquisition.

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How to cite this article;

Swochhal Prakash Shrestha, Warangkhana Chaisowwong, Orapun Arjkumpa, Mukul Upadhyaya, Pragya Koirala, Manju Maharjan, Swoyam Prakash Shrestha and Veerasak Punyapornwithaya. Temporal trend and high-risk areas of rabies occurrences in animals in Nepal from 2005 to 2018. Veterinary Integrative Sciences. 2023; 21(2): 411 - 427.