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Review article

Geospatial Analysis Applied to Epidemiological Studies of Rabies Disease: A Systematic Review

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Abstract

Rabies is a deadly zoonotic disease that remains a global health problem. The incidence of this disease is increasing, but it has not yet been overcome by various parties. The easy transmission of this disease from animals to humans necessitates the use of epidemiological analysis methods to accelerate its eradication and control. This systematic review aimed to assess the types of spatial methods used in rabies epidemiological studies published between January 2014 and April 2024. Thirty-eight studies were selected, and 28 different spatial methods were used in rabies studies during that period, with two methods being the most frequently used. Few articles have applied spatial analysis methods in rabies studies; however, whenever they were applied, they contributed to a better understanding of the geospatial diffusion of rabies. This review highlights the importance of geospatial analysis for understanding the spread of rabies, identifying hotspots, and identifying the need for more targeted and effective interventions.

Kew Words: analytical models; epidemiological studies; geospatial techniques; rabies; zoonotic disease

Introduction

Rabies is a deadly zoonotic disease that remains a global health concern, particularly in regions with low animal vaccination rates and limited access to medical care [1]. Although rabies can be prevented through vaccination and animal control measures, the disease remains widespread in many developing countries, causing thousands of deaths annually [2]– [5]. A major problem faced in rabies control is the lack of appropriate and efficient identification of patterns of disease spread. The spread of rabies is influenced by a variety of environmental and social factors, including the distribution of reservoir animal populations, animal–human interactions, and geographical conditions that facilitate or inhibit disease spread [6]. Without an in-depth understanding of how these factors interact spatially, control efforts are likely ineffective. With the development of technology and science, new methods for analyze and understanding the epidemiology of rabies have become critical for improving prevention and control strategies. Geographical factors and information from different sources and formats can be spatially combined by geographic information systems (GIS), both in epidemiology and public health; for example, several previous studies have shown that geographical factors include temperature, precipitation, and spatial distribution of rabies cases; risk estimation and spatial distribution mapping of rabies cases in different regions; and successful prediction of rabies distribution Spatial studies support rabies control practices and vaccination strategies [7]–[9]. Thus, there is an urgent need for analytical methods that can integrate epidemiological and geospatial data to produce accurate risk maps and reliable prediction models, identifying spatial patterns and incorporating individual and contextual variables, these methods can significantly contribute to reducing the social and economic impacts of rabies, including specific geographic and health disparities.

This review is relevant in the context of global rabies control, particularly in endemic regions. By understanding how geospatial analysis can be used to map the spread of rabies, how effective it is in mapping the spread of rabies, identifying rabies hotspots, and identifying the challenges faced in applying geospatial analysis to rabies epidemiological studies, authorities can design more targeted and effective interventions. Therefore, the aim of this systematic review is to analyze the role of geospatial analysis in epidemiological studies, including its types, uses, and implications for society. The results of this systematic review will not only provide guidance for researchers and health practitioners in selecting and applying appropriate methods but also serve as a basis for the development of new tools and technologies for the mapping and control of complex zoonotic diseases.

2.Methods

Systematic review registration This systematic review used the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocol guidelines [10].

The eligibility criteria

At this stage, one author sorted and collected articles containing cross-sectional, cohort, observational, and experimental data. The eligibility of an article to be included in the study went through various stages and met the following established inclusion criteria: a) the article had to discuss spatial, spatial-temporal, and spatial autocorrelation in rabies; b) it clearly presented spatial methods as part of the data analysis and results preparation; c) it was published in the last decade (2014–2024); and d) it was listed in reputable journals.

indexed by PubMed, Scopus, and Web of Science (WOS). The range of years chosen depends on the novelty of the research, and the reputation of the journal determines the credibility of the article. Articles should contain methods, workflows, and supporting data that can be processed in spatial analysis and provide clear spatial outputs in accordance with the research objectives of mapping rabies disease. The detailed article eligibility criteria must include the data analysis units, typology representation, spatial methods used, and main results of spatial data analysis. The exclusion criteria for the excluded articles included a) using other foreign languages, b) not open access, c) not only discussing rabies, d) discussing rabies but not using spatial analysis methods, and e) belonging to predatory publishers and journals. All articles that did not meet the eligibility criteria, were duplicates, were discontinued studies, or were irrelevant at this stage were excluded.

Sources of information, literature search strategies, and study selection

At this stage, one author collected and searched for appropriate literature by setting keywords, including "Spatiotemporal clustering of rabies," "spatial clustering of rabies," "spatial autocorrelation of rabies," "rabies AND spatial," and "spatial-temporal AND rabies." We used trusted databases and credible sources to search for articles that matched the topic in PubMed (MeSH terms). The PubMed (http://www.ncbi.nlm.nih.gov/PubMed) and BMC (https://www.biomedcentral.com) databases were searched. The collected articles were sorted and screened for eligibility in two stages. The first stage involved title and abstract screening, in which topics had to address rabies using a spatial and/or spatial-temporal approach and met all inclusion criteria. In the next stage, all articles relevant to the topic were screened based on the research objectives, methods, results, and conclusions. Articles that did not meet one or more of the criteria were excluded. The exclusion criteria are described in the PRISMA diagram Fig. 1. Two independent researchers conducted this process to ensure objectivity.

Data extraction

The data were extracted from selected studies using a custom-designed worksheet. The following basic information was extracted: a) basic information, including title, author, year of publication (years), and journal (name, volume, issue, pages, and journal indexing); b) study design, including study objectives, type of study used, research location, and population studied (human and animal rabies epidemiology); c) geospatial methods, including the type of geospatial data used, type of data used for analysis, software, and spatial analysis techniques chosen; and d) main results, including the main findings related to spatial or spatial temporal distribution, low spots and hotspots, level of vulnerability and/or risk of rabies in an area. The data were extracted by two independent researchers. Any discrepancies will be discussed until a consensus is reached, and a third researcher will be involved if necessary.

Quality assessment The methodological quality of each selected article was assessed using a predetermined checklist in the form of a Joanna Briggs Institute (JBI) or Newcastle–Ottawa Scale (NOS) worksheet [11]. This assessment will help to assess the reliability and validity of the findings reported in previous studies.

Data collection and analysis

Two researchers independently conducted this stage. The extracted data were descriptively analyzed to provide an overview of the characteristics of the studies included in this review. This analysis will include the frequency of use of specific geospatial methods, geographical distribution of the studies, and main patterns of findings expressed in the studies, including the title and objectives of the research. Key results from the selected studies were analyzed qualitatively to identify key themes and a narrative synthesis of the application of geospatial analysis in rabies epidemiology. The main focus of the studies included data analysis units, typology of representation, spatial methods used (geospatial methods), and key outcomes of spatial analysis in relation to rabies (contribution to understanding rabies epidemiology and the challenges faced). The results of this systematic review are reported in accordance with the PRISMA guidelines and include a PRISMA flowchart [10] to illustrate the study selection process, tables summarizing study characteristics and results, and an in-depth discussion of the implications of the findings for rabies control practice and future research.

3. Results

The results of the literature search and screening yielded 38 articles that met the inclusion and exclusion criteria. These articles were published between 2014 and 2023. The stepwise screening of articles based on these criteria is presented in the PRISMA chart and PICOS framework (Fig. 1).

Initially, 161 articles published in English between 20014 and 2024 were selected. After reading the abstracts, 83 articles were excluded because they did not satisfy the inclusion criteria. Only 38 of the other 83 articles met the review criteria. We found that some authors cited spatial analysis in the abstract but did not use a spatial method to analyze the data in the geographic information system [12]–[14]. For example, some articles have incorporated the term “spatial” but used fluorescence micro-optical sectioning tomography (fMOST), as applied to neurologic tissue [14]. Furthermore, a logistic regression model was used to investigate sociospatial information [12] and to create a new application for detecting dog rabies as a graph-based evidence synthesis approach for detecting outbreak clusters [13]. A comparison of the spatial analysis methods used in the selected articles is given in Table 1.

No.	Reference	Spatial Method	Objectives of spatial analysis
1	[7]	Kernel density estimation [15], SaTScan [16].	To describe spatial and temporal patterns of rabies. To discuss effectiveness of oral rabies vaccination campaigns in targeted oblasts. To identify geographical territories with zero rabies cases among animals. To detect spatial-temporal clusters of rabies cases using space-time permutation model. To compare densities of disease cases on an annual basis.
2	[8]	Spatial methods include Moran's I, Geary's C [17], and Getis-Ord's G [18].	To visualize disease data using GIS tools to show spatial distribution. To study relationship between disease incidence and environmental factors geographically. To analyze spatial dynamics to understand spread and develop control strategies.
3	[9]	Geostatistics estimate and predict [19].	To determine relationship between temperature, precipitation, and rabies spatial distribution. To identify high-risk areas for rabies outbreaks using geographic information systems. To predict spatial risk and distribution of rabies cases in livestock.
4	[20]	Moran's global index and Cluster and Outlier Analysis [17]	To identify clusters of high and low values in rabies cases. To classify governorates based on the number of rabies or PEP cases.
5	[21]	SaTScan [16], Global Polynomial Interpolation and Contour tool [22].	To identify high-risk clusters and spatial expansion of human rabies cases. To analyze spatial distribution and clustering of human rabies occurrences. To determine trends in the spread speed of human rabies cases.
6	[23]	Bayesian hierarchical spatiotemporal model [24]	To understand spatiotemporal variation of rabies. To examine impacts of environmental, economic, and demographic factors on rabies
7	[25]	Monte Carlo simulations [26]	To assess spatial association between rabid dogs and urban structures. To determine if rabid dogs are closer to water channels than expected.
No.	Reference	Spatial Method	Objectives of spatial analysis
			To analyze spatial clustering of rabid dogs.
8	[27]	Average Nearest Neighbor (ANN) method [28].	To determine disease distribution patterns for effective control strategies. To analyze spatial data to identify clustering, dispersion, or randomness. To measure distances between objects to understand distribution patterns.
9	[29]	Negative binomial regression [30], Z-score analyses [31].	To assess behavior and status of raccoon variant rabies virus cases. To examine virus in non-raccoon hosts. To evaluate impact of oral rabies vaccine distribution
10	[32]	Spatial scan statistics [16], Poisson regression modeled variables [33]	To identify clusters of canine rabies cases. To evaluate the influence of social determinants on canine rabies incidence. To create a risk map for canine rabies based on social factors
11	[34]	Statistical modeling of cointegration techniques [35]	To Verify effect of weather components on rabies incidence. To Establish long-run relationship among reported rabies cases, temperature, and precipitation. To Guide local health officials in formulating preventive strategies for rabies control
12	[36]	Generalized Additive Models [37], Two-dimensional LOESS [38], Permutation tests [39].	To identify spatial patterns in data for vaccination campaign planning. To Assess clustering of unvaccinated dogs to improve rabies prevention strategies. To Analyze geolocation impact on canine vaccination. To Maintain confidentiality by avoiding public availability of geographic coordinates.

13	[40]	Moran's index [17], Chi- squared tests [41]	To Compare Myotis species identification using morphological keys and genetic identification. Characterize temporal and spatial trends of bat RABV. Assess risk factors for bat RABV infection by circumstances of encounter.
14	[42]	Used discrete Poisson spatial model [43], Using space-time permutation model [44]	To Identify clusters of high rabies incidence in specific regions.
No.	**Year**	**Number of Article** **Periodical**	**Quartile**
			To analyze spatial clustering of rabid dogs.
8	[27]	Average Nearest Neighbor (ANN) method [28].	To determine disease distribution patterns for effective control strategies. To analyze spatial data to identify clustering, dispersion, or randomness. To measure distances between objects to understand distribution patterns.
9	[29]	Negative binomial regression [30], Z-score analyses [31].	To assess behavior and status of raccoon variant rabies virus cases. To examine virus in non-raccoon hosts. To evaluate impact of oral rabies vaccine distribution
10	[32]	Spatial scan statistics [16], Poisson regression modeled variables [33]	To identify clusters of canine rabies cases. To evaluate the influence of social determinants on canine rabies incidence. To create a risk map for canine rabies based on social factors
11	[34]	Statistical modeling of cointegration techniques [35]	To Verify effect of weather components on rabies incidence. To Establish long-run relationship among reported rabies cases, temperature, and precipitation. To Guide local health officials in formulating preventive strategies for rabies control
12	[36]	Generalized Additive Models [37], Two-dimensional LOESS [38], Permutation tests [39].	To identify spatial patterns in data for vaccination campaign planning. To Assess clustering of unvaccinated dogs to improve rabies prevention strategies. To Analyze geolocation impact on canine vaccination. To Maintain confidentiality by avoiding public availability of geographic coordinates.

13	[40]	Moran's index [17], Chi- squared tests [41]	To Compare Myotis species identification using morphological keys and genetic identification. Characterize temporal and spatial trends of bat RABV. Assess risk factors for bat RABV infection by circumstances of encounter.
14	[42]	Used discrete Poisson spatial model [43], Using space-time permutation model [44]	To Identify clusters of high rabies incidence in specific regions.

No.	Reference	Spatial Method	Objectives of spatial analysis
			To Determine areas with significant aggregation of rabies cases in dogs.
15	[45]	WGS techniques [46]	To identify genetic relationships of RABV variants, reservoirs, and spatial origin. To generate novel data for future investigations. To monitor virus evolution, transmission, and emergence of relevant genetic mutations
16	[47]	Phylogeny reconstructed by maximum likelihood and Bayesian methods [48]. Beast and SPREAD software[49]	To understand evolutionary history and spatial temporal dynamics of rabies virus. To determine evolutionary rates and phylogeographic using Beast and SPREAD software. To illustrate the evolution history and phylogeographic of RABV in badgers.
17	[50]	Continuous time and space [51].	To identify patterns in time and space for fox rabies control. To focus on disease dynamics in continuous time and space domains. To highlight potential risk areas and need for effective rabies vaccination
18	[52]	Spatially explicit individual- based model [53]	To investigate how spatiotemporal variation in wildlife host home range movement, implemented as home range size variation, affects the spatial spread, persistence, and incidence of wildlife disease and vaccination effectiveness.
19	[54]	Used Moran Index [17] and Moran Local Index [55].	To identify clusters of inadequate postexposure human rabies procedures spatially. To characterize exposure to the disease and its risk factors geographically. To provide epidemiological evidence for health policy planning and decision-making

No.	Reference	Spatial Method	Objectives of spatial analysis
20	[56]	Bayesian Markov Chain Monte Carlo (MCMC) simulation in the BEAST [57]	To infer viral phylogenetic relationships in space and time. To gain insights into the contribution of host population to viral spread.
21	[58]	Bayesian regression models Integrated Nested Laplace Approximations (INLA) [59]	To assess impact of accessibility on yearly rate of [48], Used PEP patients. To generate risk map to identify optimal locations for future centers. To consider travel time to nearest IPC center as primary exposure variable. To investigate spatial and temporal scales for PEP patient predictions.
22	[60]	Cross-K function [61].	To analyze spatial clustering between feeding points and dog rabies cases. To investigate the spatial association of stray dog feeding behavior and rabies cases. To simulate the spread of rabies virus among dogs in different subpopulations
23	[62]	Generalized Additive Models (GAM) [37], SaTScan [16].	To identify risk factors for rabies To predict spatial risk areas for rabies spread To quantify association between monthly rabies occurrences and explainable variables. To Strengthen surveillance system in high-risk areas.
24	[63]	DOT map cartograms [64]	To evaluate statistical association between administrative divisions and rabies cases. To use DOT density maps for comparing distribution of rabies cases.
25	[65]	Dynamic patch occupancy [66].	To predict spatiotemporal dynamics and spread rates in wildlife diseases. To understand factors driving spread like seasonality, transmission distance, and infection density. To estimate transmission distance, rates of spatial spread, and direction of invasion.
26	[67]	Logistic regression [68]	To identify trends in animal bites and rabies incidence spatially. To analyze spatial distribution of animal bites and pets vaccinated. To determine regions with higher incidence of animal bites. To assess spatial patterns of rabies-related human mortality.
27	[69]	Kernel function used for spatial distribution analysis [70], Multicriterion Analytical Hierarchy Process technique [71].	To identify high-risk areas for bovine/human rabies transmitted by bats. To analyze spatial distribution of rabies cases. To assess association with independent variables. To Evaluate environmental and socioeconomic variables for dynamic epidemiological mosaic.
28	[72]	Smartphone technology directed [73]	To identify clusters of rabies cases for targeted interventions. To analyze spatial distribution of rabies cases for epidemiological insights. To understand geographic patterns of rabies transmission for control strategies.
29	[74]	SaTScan [16], Choropleth maps[75], Phylogenetic tree [76]	To identify spatial clusters of dog rabies cases for analysis To understand spatial relationships between animal and human rabies cases To compare positivity rates in different provinces using spatial analysis
30	[77]	General Method of Moments (GMM) [78], Spatial autocorrelation addressed [79]	To quantify socioeconomic and climate factors in spatial distribution of rabies. To understand spatial heterogeneity and spatial dependence effects in regression models. To analyze the influence of climatic and socioeconomic factors on rabies spread. To compare traditional regression models with aggregation model for better performance.

31	[80]	Chi-squared tests [41] Moran's index [55]	To assess geographic and temporal trends in human and animal rabies cases. To identify provinces with higher bite rates and human rabies cases. To Determine the distribution of human suspect rabies cases throughout the country.
32	[81]	Kriging method [82], Geostatistics[19]	To identify geographic clusters of rabies for control strategies. To understand spatial distribution patterns of animal rabies. To highlight landscape determinants of the disease (rural, urban, suburb).
33	[83]	Descriptive statistics [84]	To describe human rabies incidence and spatial distribution. To investigate secondary cases and suggest pre- exposure prophylaxis for high-risk populations
34	[85]	Inverse Distance Weighted Interpolation [86], Getis-Ord's Gi statistic [18]	To identify risk factors and patterns of human rabies exposure. To analyze spatial distribution of human rabies exposures using GIS tools.

No.	Reference	Spatial Method	Objectives of spatial analysis
			To provide insights for cost-effective disease prevention and control measures.
35	[87]	Quasi-Binomial Regression Model [88]	To assess current risk of rabies spread. To evaluate efficacy of rabies contingency plans. To analyze influence of dog owner responses to rabies incursions.
36	[89]	Spatial method [90]	To clarify epidemiology of rabies. To evaluate factors influencing spread of rabies. To assess effects of rabies control and preventive measures.
37	[91]	Chi- squared tests [41]	To identify spatial patterns, relationships, and trends in dog biting incidents. To determine the association between dog bites and neighborhood characteristics. To analyze the spatial distribution of dog bites based on socioeconomic factors.
38	[92]	Kernel density estimation [15]	To visualize bat collection points and distribution patterns. To estimate density contribution of each point in the analysis. To identify statistically important areas for bat rabies surveillance. To analyze seasonal variation in bat removal requests and testing samples. To assess the spatial relationship between warmer months and bat activity.

Table 1: Review of the spatial analysis methods used in the selected articles.

Year of studies and publication

Variations were reported in the period studied. Most published studies involved an analysis of data covering one year or more. Generally, the articles used data that had been collected one to six years before publication. Approximately 53. 8% of the studies published used data collected for 1 to 5 years and 17. 9% used data collected for 6 to 10 years. Furthermore, more than 82. 1% of the studies were published less than five years after the event occurred and only 2. 6% of the studies used data collected more than 30 years before publication. Few papers using spatial analysis [25], [27], [47], [50], [56], [65], [69], [89], were published between 2014 and 2017, but since 2018, the number of papers based on geospatial studies has increased. Approximately 60% of the relevant papers were published after 2018 [7], [8], [34], [36], [40], [42], [45], [52], [54], [58], [60], [62], [9], [63], [67], [72], [74], [77], [80], [81], [83], [85], [87], [14], [91], [92], [20], [21], [23], [27], [29], [32] Table **2**.

No.	Year	Number of Article	Periodical	Quartile
1	2014	1	Emerging Infectious Diseases	https://wwwnc.cdc.gov/eid/about Scopus Quartile 1 (Q1)
2	2015	1	Geospatial Health	https://www.geospatialhealth.net/ Scopus Quartile 3 (Q3)
3	2016	3	PLOS Neglected Tropical	https://journals.plos.org/plosntds/ Scopus Quartile 1 (Q1)
			PLOS ONE journal	https://journals.plos.org/plosone/ Scopus Quartile 1 (Q1)
			Molecular Sciences MDPI	https://www.mdpi.com/journal/ijms Scopus Quartile 1 (Q1)
4	2017	2	PLOS Neglected Tropical Diseases,	https://journals.plos.org/plosntds/ Scopus Quartile 1 (Q1)

			Tropical Medicine and Infectious Disease.	https://www.mdpi.com/journal/tropicalmed Scopus Quartile 2 (Q2)
5	2018	7	PeerJ,	https://peerj.com/ Scopus Quartile 2 (Q2)
			PLOS ONE, PLOS ONE,	https://journals.plos.org/plosone/ Scopus Quartile 1 (Q1)
			BMC Infectious Diseases,	https://bmcinfectdis.biomedcentral.com/ Scopus Quartile 1 (Q1)
			Journal Epidemiologia e servicos de saude,	https://www.scielo.br/j/ress/ Scopus Quartile 2 (Q2)
			Epidemiology and Infection journal,	https://www.cambridge.org/core/journals/epidemiology- and-infection Scopus Quartile 2 (Q2)
			BMC Veterinary Research	https://bmcvetres.biomedcentral.com/ Scopus Quartile 1 (Q1)
6	2019	5	Frontiers in Veterinary Science,	https://www.frontiersin.org/journals/veterinary-science
				Scopus Quartile 1 (Q1)
			Geospatial Health,	https://www.geospatialhealth.net/ Scopus Quartile 3 (Q3)
			PLOS Neglected Tropical Diseases,	https://journals.plos.org/plosntds/ Scopus Quartile 1 (Q1)
			Journal of the Brazilian Society of Tropical Medicine,	https://www.scielo.br/j/rsbmt/ Scopus Quartile 3 (Q3)
			Ethiopian Veterinary Journal.	https://www.ajol.info/index.php/evj Scopus Quartile 1 (Q1)
7	2020	5	PLOS ONE,	https://journals.plos.org/plosone/ Scopus Quartile 1 (Q1)
			Preventive Veterinary Medicine,	https://www.sciencedirect.com/journal/preventive-veterinary-medicine Scopus Quartile 1 (Q1)
			Journal of Animal Ecology,	https://www.scirp.org/journal/oje/?utm Scopus Quartile 1 (Q1)
			Frontiers in Veterinary Science,	https://www.frontiersin.org/journals/veterinary-science Scopus Quartile 1 (Q1)
			PLOS Neglected Tropical Diseases	https://journals.plos.org/plosntds/ Scopus Quartile 1 (Q1)
8	2021	7	Veterinary Medicine and Science,	https://onlinelibrary.wiley.com/journal/20531095 Scopus Quartile 2 (Q2)
			Veterinary World,	https://www.veterinaryworld.org/ Scopus Quartile 2 (Q2)
			viruses MDPI Journal,	https://www.mdpi.com/journal/viruses Scopus Quartile 1 (Q1)
			PLOS Neglected Tropical Diseases	https://journals.plos.org/plosntds/ Scopus Quartile 1 (Q1)
			Tropical Medicine Infection Disease	https://www.mdpi.com/journal/tropicalmed Scopus Quartile 2 (Q2)

No.	Year	Number of Article	Periodical	Quartile
			PLOS Neglected Tropical Diseases,	https://journals.plos.org/plosntds/ Scopus Quartile 1 (Q1)
			Heliyon Journal	https://www.cell.com/heliyon/home Scopus Quartile 1 (Q1)
9	2022	6	Journal of Geospatial Health,	https://www.geospatialhealth.net/ Scopus Quartile 3 (Q3)
			Environmental Research and Public Health,	https://www.mdpi.com/journal/ijerph Scopus Quartile 2 (Q2)
			Clin Transl Med,	https://onlinelibrary.wiley.com/journal/20011326 Scopus Quartile 1 (Q1)

			PLOS Neglected Tropical Diseases,	https://journals.plos.org/plosntds/ Scopus Quartile 1 (Q1)
			NATURE COMMUNICATIONS,	https://www.nature.com/ncomms/ Scopus Quartile 1 (Q1)
			PLOS Neglected Tropical Diseases.	https://journals.plos.org/plosntds/ Scopus Quartile 1 (Q1)
10	2023	2	Tropical Medicine and Infectious Disease (MDP),	https://www.mdpi.com/journal/tropicalmed Scopus Quartile 2 (Q2)
			International Journal of Infectious Diseases	https://www.scirp.org/journal/aid/?utm_campaign Scopus Quartile 1 (Q1)

Table 2: Total articles by year and periodical.

Epidemiological information on human and animal rabies

Nine of the studies included in this review applied spatial methods to epidemiological information about human and animal rabies [9], [20], [58], [63], [69], [74], [80], [87], [91]; nine articles analyzed only epidemiological information about human rabies [8], [21], [23], [54], [72], [77], [83], [85], [89] and 21 articles focused solely on the epidemiology of animal rabies [7], [14], [45], [47], [50], [52], [56], [60], [62], [65], [67], [81], [25], [92], [27], [29], [32], [34], [36], [40], [42].

In terms of the geometric or shape representation of data, studies have primarily used polygons and point data. The polygons were used to represent administrative frontiers, such as neighborhoods, districts or other administrative frontiers, and the points were used to represent cases of rabies, households, and animal (dog, cat, bats, etc.) traps. There was no predominant type related to the topology utilized because it was common to use more than one type of topology in the articles. For example, often, data are collected at the household level, but for analysis purposes, they are aggregated into areas.

Spatial units

Among the articles selected, 12 different primary units of analysis were identified. The most commonly used primary unit of analysis was more than one unit of spatial analysis; for example, counties; cities; provinces; districts; human and animal rabies cases; municipalities; administrative towns; cities; rivers; lakes;

departments; and villages were applied in fifteen articles or approximately 38% of the published studies [9], [21], [72], [80], [81], [89], [92], [27], [32], [36], [40], [42], [58], [62], [67]. Human and rabies cases were used as primary units in seven studies [14], [50], [52], [60], [63], [65], [77], and municipalities were used in four studies [54], [69], [74], [83]. Two studies [23][7] used the province as the unit of analysis. Other studies have used the region as an analysis unit [47], [56]. In two studies, city data were used [20], [34]. The term "state" was applied in two studies [45], [87], "administrative districts" was used in one study [85], "the counties" was used in one study

[29], "the global units" was used in one study [8], and "neigborhood" was used in one study [91]. Furthermore, the line (water channel) unit was used in one study [25].

Methods of spatial analysis applied in rabies studies

Twenty-eight different spatial methods used to analyze the rabies data were found in the articles. However, some were more common than others. The methods used in the selected papers are listed according to the topology of the data used Table 1.

Spatial analysis of points

In the analysis of point data, the method used most frequently, in 5 papers [32], [42], [62], [72], [74], was spatial scan statistics (SaTScan) [16]. The Moran's index statistic [55], was used in two papers [8], [77]. K-D analysis [15], was applied in a separate study [92] and in another study [7], standard distances and a space-time permutation model were applied. Two papers [23], [58], used only Bayesian models [48]. The Getis-Ord Gi statistic [18], was used in two studies [8], [85].

The average nearest neighbor (ANN) [28], was applied in one paper [27]. The discrete Poisson spatial model (DPS) [43] was applied in one study [42], and the cross-K function [61] was applied in two papers [36], [50]. The kriging method [82] and geostatistical methods [19] were applied in two papers [9], [81]. Monte Carlo simulations [26] and the L function [93] were used in one paper [25]. The standard distances [94] and space- time permutation model [44] were applied in one paper [7]. In one paper [8], Geary's Contiguity Ratio [95] was used. The analytical hierarchy process (AHP) technique [71] was applied in one [69] study, the R for accuracy test [96] was used in another study [52], and DOT map reshaping [64] was applied in one study [63]. Furthermore, the fMOST and scRNA-seq techniques reveal the 3D rabies virus (RABV) distribution in the brain [97] and were used in one study [14]. Finally, the descriptive statistical model [84] was applied in one study [83].

Spatial analysis of area data

The spatial scan statistics (SaTScan) method [16] is the most common method used for analyzing polygon data [32], [42], [72], [74]. Another commonly used method was the global Moran index [55], which was applied in three studies [20], [54], [77]. The Cross-K function [61] was applied in two studies [50], [60]. Furthermore, generalized additive models (GAMs) [78] were applied in two studies [36], [62]. The Monte Carlo method [26] was applied in one study [25], the average nearest neighbor (ANN) method [28] was applied in another [27], the kriging method [82] was applied in one study [81], the Bayesian regression models [48] were applied in one study [58], and the Getis-Ord Gi statistic [18] was applied in another [91].

Software programs used for spatial analysis of rabies cases

Some articles did not report which software had been used to perform the spatial analysis of the data. Furthermore, in some cases, the method of spatial analysis was not referenced; instead, the focus was on the set of operations utilized. For example, it was clear in every article that different software programs had been used; in some cases, one software program was used to create geographical coordinates (latitude and longitude), and another was used specifically to perform spatial analysis. The software programs used in the selected articles are given in Table 3. The most commonly used methods were ArcGIS, R software, GeoDa, TerraView, Moran's index and MapInfo. Several other software programs, for example, SaTScan, Terrasse, BioEdit, and ClustalX version 1.8, have been used. MegAlign software version 5. MEGA version 5, R, the stpp- package cellular automata (CA) and other customized versions were used but not as often.

No.	Year	Software	Number of studies
1	2014	BioEdit software, ClustalX version 1.8.	1
		MegAlign software version 5.	1
		MEGA version 5	1
2	2015	R and the stpp-package	1
		Cellular automata (CA)	1
3	2016	Kernel function	1
		TerraView 4.2.2	1
		ArcGis 10.0	1
		Beast and SPREAD	1
		Maximum likelihood and Bayesian	1
4	2017	R software	1
		Geographic Information System (GIS)	1
		ArcGIS 10.3	1
		Dynamic patch-occupancy model	1
5	2018	R (version 3.4.2) with glmmADMB package	1
		The glmmADMB package	1
		SaTScan(tm) v8.0 software	1
		SAS 9.4 and Microsoft Excel 2013	1
		GMM adopted for unbiased estimation with spatial autocorrelation.	1
		Moran's I statistic	1
		TabWin 32, Epi Info 7.1, and Microsoft Excel 2010.	1
		Individual-based model on a 1-by-1 km grid.	1
		Spatially explicit transmission model developed at 1 km2 grid scale	1
		Minitab software for descriptive statistics and linear regression analysis.	1
		Kernel density estimation.	1
6	2019	R package malariaAtlas	1
		Rapid Extractor of Climatological Information III (ERIC III).	1

No.	Year	Software	Number of studies
		Geographic Information Systems (ArcGIS) software	4
		TerraView 4.2.2	1
7	2020	Moran's index.	1
		Spatial analysis conducted using Moran's I statistic for geographic trends	1
		Cross-K function.	1
		Metapopulation analysis.	1
		SEIR model.	1
		Spatially explicit individual-based model.	1
		Sensitivity analyses conducted	1
		SaTScan software utilized for spatial and spatiotemporal analysis.	1
		No information	1
		Moran's global index and spatial autocorrelation by Cluster and Outlier Analysis	1
8	2021	Package "spdep" of R software for spatial analysis	1
		ArcGIS was used for spatial analysis	4
		SaTScan.	1
		Ordinary Kriging regression.	1
		Kriging method applied to estimate missed data in reporting process.	1
		Generalized Additive Models (GAMs) were used for spatial analysis	1
9	2022	Dynamical models and phylogenetic analysis	1
		ArcGIS	2
		SaTScan version 9.3	1
		fMOST and single-cell RNA sequencing techniques	1
		Spatiotemporal Bayesian regression models	1
		Bayesian statistics.	1
		R code	1
		SaTScan.	2
10	2023	ArcGIS software	2

	Stata version 17	1

Table 3: List of software used each year

4. Discussion

Despite place being a fundamental component of epidemiological investigations, the small number of papers found may indicate that the use of spatial analysis in studies of rabies is still uncommon. Among the possible reasons that may hinder the application of spatial analysis in the data analysis of rabies infections is the lack of health information systems that produce georeferenced human and animal epidemiological information, that is, the appropriate scales of analysis.

As of 2018, there was a significant increase in the number of articles that addressed the application of spatial analysis in studies of rabies. 60 % of the published articles were found from that year on, perhaps due to the increased severity of the rabies epidemics observed during this period. This increase could also be result of the need to develop new approaches to rabies research, to better understand the dynamics of disease transmission and to formulate strategies to minimize its effects. Among the works selected, there was a significant time interval between the occurrence of events (rabies cases), or even between the execution of virological and human and animal (zoonotic) surveys, and the publication of the results of spatial analyses. This time lag might have been due to the natural flow of research, but it might also reflect the complexity and difficulties involved in conducting spatial analyses in countries where rabies is endemic. The existence of such a longtime interval between the collection of human and animal epidemiological information and the analysis and dissemination of results can lead to bias against the early detection of epidemics [98]. Therefore, there is a reduction in the ability to identify surveillance sites that require public health action.

Although most studies of rabies using spatial analysis were based on data from countries where the disease is endemic, the studies themselves were conducted elsewhere. The exception is the USA, which has developed most of the spatial analyses, according to articles published in the countries themselves. Among the countries studied, 26% of the articles were from Brazil and China, followed by Colombia, Peru, and Tunisia, which are often targeted for research because they highlight geographical disparities in research focus and capability; however, countries with geographical disparities in rabies, such as Timor-Leste [99], Indonesia [100], and others that are highly zoonotic areas, have not been widely reported. Therefore, geospatial analysis should be performed in other areas with widely reported zoonotic diseases, particularly rabies cases.

Furthermore, more than one unit of spatial analysis has been the most commonly used spatial unit, followed by human and rabies cases as primary units and municipalities. This could be due to the actual characteristics of the epidemiological studies of human and animal rabies, which often focus on the surrounding areas (e.g., counties, cities, provinces, districts, human and animal rabies cases, municipalities, administrative towns, cities, rivers, lakes, departments, villages, etc.) because of the ecological characteristics associated with the spread of animals (dogs, mice, bats, etc.) [3], [6], [74], which are the transmitter agents of rabies disease. Twenty-eight different methods of spatial analysis were found; however, only two of them were used frequently. In analyzing the point data, the most commonly used method was the spatial-time scan (SaTScan) method. These methods essentially impose circles of different sizes (from zero to a defined proportion of the population size) on the geographic area, and for each circle, a likelihood ratio statistic is computed based on the number of observed and expected cases [16].

For the analysis of polygon data or areas, the most widely used indicator is StatsCan (spatial-time scan), and Moran's global statistic is the most common way of measuring the degree of spatial autocorrelation in area data [101], perhaps because of the ease of application and interpretation of results; the greater availability of free ArcGIS, R software, GeoDa, Rereview, Moran's index and MapInfo; or the lack of health information on more highly detailed scales. The other 25 methods of analysis were each used by only one or two articles and were used as a complement to traditional methods of statistical analysis.

Some of the methods might have been more commonly used due to their greater popularization because of the ease of access, as generally, they are implemented in commercial software with great diffusion capacity and easy-to-handle friendly interfaces, as well as in the public domain, which has a larger number of courses and tutorials that assist the user in their use. On the other hand, although some of the methods least commonly used may be available, both in the software of the public domain and in commercial software, they have as yet been little disseminated and present little didactic material, often having relatively unfriendly interfaces that make their manipulation on the part of users who have little familiarity with special data difficult. Although they are commercial software, ArcView/ArcGIS and MapInfo are among the software programs most commonly used, probably because they present more friendly interfaces than do the free software programs and rely on a wide range of programs for the dissemination of and training in their use. On the other hand, although they are free (software) programs, GeoDa and Tera view are also frequently used, probably because they make the methods commonly used in spatial analyses in public health available free, together with didactic material, and are widely represented at technical and scientific events [102]– [104].

Despite these considerations, it is pertinent to point out that, regardless of the sophistication of the method used, the results shown in the papers pointed to the great utility of spatial analysis for understanding the epidemiology of human and animal rabies cases on different continents and in different geographical areas. Furthermore, the results have shown that methods such as the spatial-time scan (SaTScan) method and Moran's global method can quickly produce efficient information regarding the location of clusters of rabies cases and hotspot areas of transmission [16], [44], [101]. Such information can be a powerful tool for monitoring rabies transmission at the local level. Finally, despite the development of spatial analysis methods applied in epidemiological studies, these methods are rarely used in studies of rabies. However, the identification of spatial patterns in most of the articles discussed above confirms the usefulness of these techniques and the need for the development and application of advanced spatial analysis beyond the limits of visualization.

Some spatial analysis methods should be used in conjunction with conventional methods, such as the control diagrams currently used by public health programs to identify rabies risk [105]. The use of these methods to advance scientific knowledge on the dynamics of rabies transmission and its spatial diffusion could certainly be incorporated into current surveillance strategies and may contribute to reducing social costs by incorporating both the individual and contextual variables associated with rabies transmission.

4. Conclusion

The types of spatial methods used in rabies epidemiological studies published between January 2014 and April 2024. From the articles selected, there were 28 different spatial methods used in rabies studies during that period, with two methods being the most frequently used. Few articles have applied spatial analysis methods in rabies studies; however, whenever they were applied, they contributed to a better understanding of the geospatial diffusion of rabies. This review highlights the importance of geospatial analysis for understanding the spread of rabies, identifying hotspots, and identifying the need for more targeted and effective interventions. It also suggests that integrating these methods can improve our understanding of rabies transmission dynamics and provide more effective surveillance and intervention strategies. There is a clear and urgent need to develop and apply spatial analysis techniques for rabies research and eradication in the region.

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