



Comprehensive assessment of lumpy skin disease prevalence across Asia and African countries: A systematic review and meta-analysis

ASHWINI M¹, SURESH K P¹, S S PATIL^{1✉}, DIVAKAR HEMADRI¹, BALDEV RAJ GULATI¹,
N N BARMAN² and AKSHATA NAYAK³

ICAR-National Institute of Veterinary Epidemiology and Disease Informatics, Yelahanka, Bengaluru,
Karnataka 560 064 India

Received: 4 March 2024; Accepted: 9 July 2024

ABSTRACT

Lumpy Skin Disease (LSD) stands out as one of the economically significant ailments affecting both small-scale farmers and the broader livestock industry. To gauge its prevalence across Asia and Africa, this study employs a rigorous methodology combining systematic review, and meta-analysis, accounting for heterogeneity. Adhering to the guidelines set forth by the cochrane collaboration's preferred reporting items for systematic reviews and meta-analysis, present initial search sifted through approximately 6,000 articles spanning from 1990 to 2022, using carefully crafted combinations of keywords; Boolean operators, asterisks, and quotation marks. After meticulous assessment for quality bias, employing inclusion and exclusion criteria, 52 publications were included in present study for analysis. The methodology involved in current study utilizing scientometric tools to determine LSD prevalence, with a median sample size of 293 across various studies, predominantly focusing on cattle and buffaloes. Meta-analysis outcomes were dissected based on parameters such as study period, sample size, tests employed, continents, and species, with samples stratified into two to three categories based on medians for heterogeneity assessment. Meta-analysis unveiled a pooled prevalence rate of 14% in Asia and Africa. The subgroup analysis found an 11% prevalence in Asia and Africa constituted 21%. Clinical observation showed a 19% prevalence followed by other tests and PCR with 12 and 13%, respectively. The results underscore the necessity for effective strategies to control and prevent LSD spread, mitigating its economic impact on the livestock industry. This collaborative and comprehensive assessment is crucial in combating the widespread dissemination of LSD and offers valuable insights for policymakers, veterinarians, and stakeholders in the livestock sector.

Keywords: Africa, Asia, LSD, Meta-analysis, Meta-regression, Prevalence

Lumpy skin disease is an acute, subacute, viral disease of cattle accompanied by fever, depression, and a low mortality rate that results in low milking of firm, constrained skin nodules that undergo necrosis (Abdullatif 2021). The economic impact of LSD is severe, causing significant losses in the livestock industry (Selim *et al.* 2021a). The World Organization for Animal Health (OIE) has recognized the disease as notifiable (Diab *et al.* 2021), (Hasib *et al.* 2021) and a transboundary animal disease due to economic consequences and potential for spreading across border (Gari *et al.* 2008, albayrak *et al.* 2018, Biswas *et al.* 2020, Ahmad *et al.* 2021).

The prevalence of LSD was documented in Turkey, Ethiopia, Egypt, North Eastern Ethiopia, Bangladesh, Iraq,

Myanmar, and India, inflicting considerable economic losses (Fayad 2017) in commercial cattle production (Issimov *et al.* 2022). Numerous studies have been carried out to determine the prevalence of LSD in various animal species across geographical regions. The investigations highlighted the varying frequency of LSD in a given area, which may be caused by several variables, including the use of diagnostic assays (PCR, ELISA, etc) and study methods. Considering the standards mentioned above, the current study aims to evaluate the disease prevalence across Asia and African countries, a systematic review was conducted which focused on implementing intervention strategies for the prevention of LSD by utilizing meta-analysis. The findings of multiple searches were combined to synthesize the data and derive comprehensive insights (Normand *et al.* 2005). The studies published from 1990-2022 were included after being authenticated by two independent authors specifically to evaluate the decadal change/trend in the disease prevalence, devising surveillance and control strategies, economic impact, advancing vaccine development, and understanding the

Present address: ¹ICAR-National Institute of Veterinary Epidemiology and Disease Informatics, Yelahanka, Bengaluru, Karnataka. ²College of Veterinary Sciences, Assam Agricultural University, Jorhat, Assam. ³Institute for Social and Economic Change, Bengaluru, Karnataka. ✉Corresponding author email: sureshkp97@rediffmail.com

disease from a One Health perspective. Moreover, it aids in identifying the existing knowledge gaps that might require further investigation (Sargeant and O'Connor 2014). Thus, knowledge of the prevalence percentage is important to mitigate the disease spread and economic loss. Our study lays a strong foundation for LSD control, providing critical insights to policymakers, veterinarians, and researchers in understanding its distribution, and helping prioritize veterinary healthcare, prevention, and policy implementation.

MATERIALS AND METHODS

This study conducted a thorough literature search across databases to assess LSD prevalence in cattle, buffaloes, sheep, and goats in Asia and African countries. Approximately 6,000 articles from 1990 to 2022 were screened, with only peer-reviewed publications included. The systematic approach, illustrated in Fig. 1, ensured methodological rigor. Studies reporting LSD prevalence using established diagnostic methods were included, excluding those evaluating LSD control strategies. Relevant articles were identified following PRISMA guidelines, supplemented by back-reference searches using Zotero 5.0 and Rayyan QCRI (Shamseer *et al.* 2015). Our study focused on LSD prevalence across Asia and African countries. Duplicate papers were checked, and data on bibliographic details, demographics, and study results were extracted independently. Meta-analysis standards were followed, and various confirmatory tests were employed. Two hundred and fifteen English articles, including journals and theses for literature review were identified in present study. These underwent strict screening criteria. Articles do not provide data on LSD prevalence, and studies predating 1990 were omitted to maintain analytical integrity. The researcher extracted data on the authors of

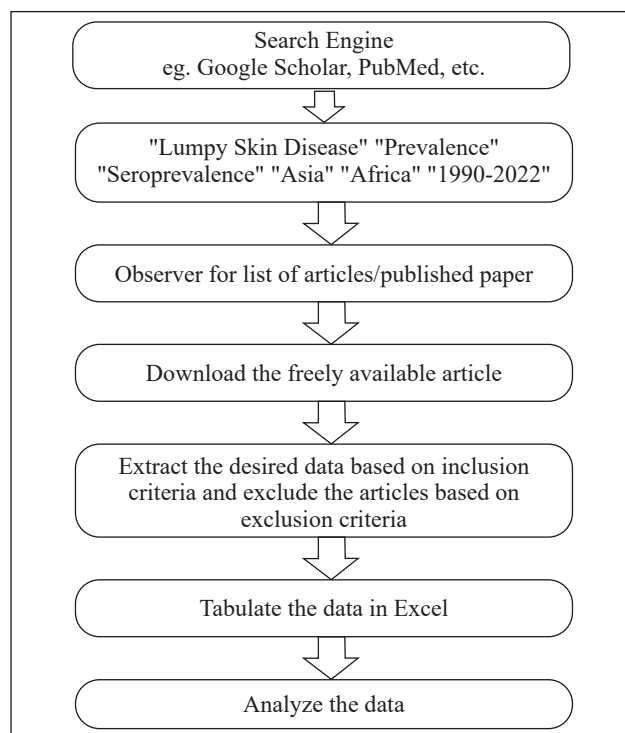


Fig. 1. Unveiling insights through search strings and filters in the Google Scholar database.

the article, study period, sample size, detection techniques, and countries. Supplementary data on LSD prevalence percentage, infection rates, mortality, morality, and morbidity were incorporated to assess the accuracy. The final screening resulted in 52 suitable articles included for analysis (Fig. 2).

Quality assessment of studies: Inter-rater agreement is crucial when assessing the quality of concepts. Aiken's V was proposed to summarize agreement ratings from

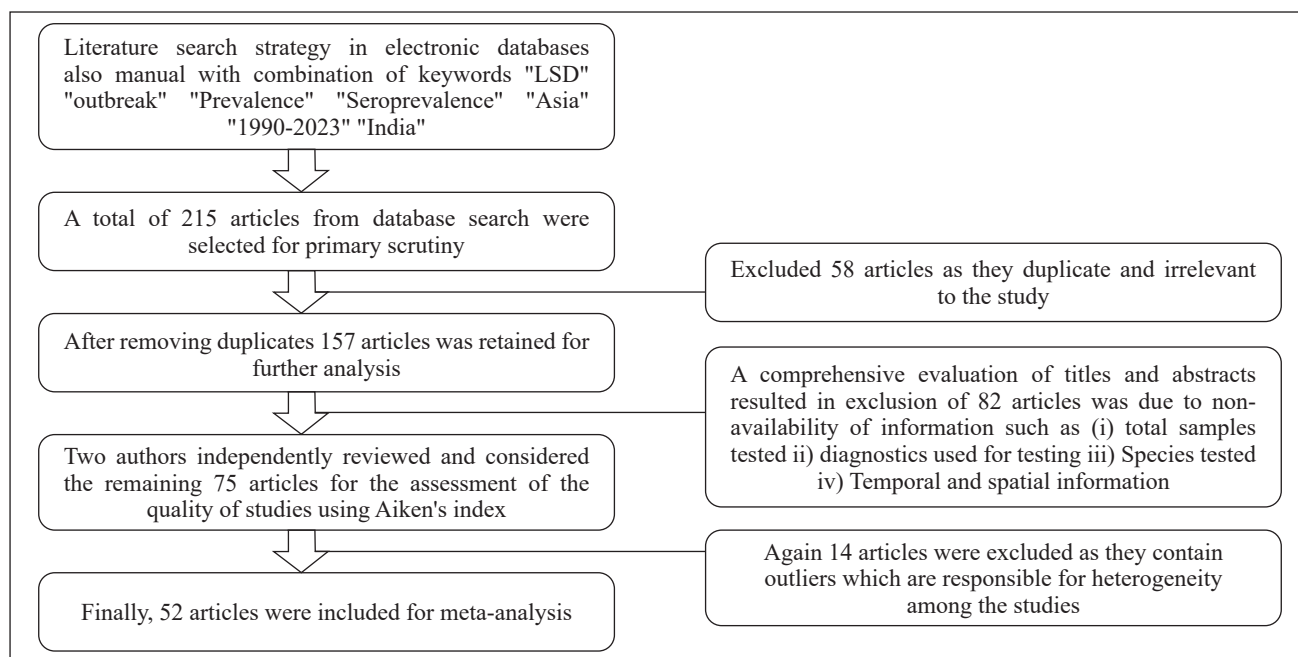


Fig 2. Schematic illustration of articles selection for systematic review.

Table 1. Interrater agreement testing between two raters in using the risk of bias tool

Validation procedure	Author 1*	Authors 2*	KAPPA (95 % CI)
<i>External validation</i>			
Was the study's target population representative of the national population concerning relevant variables?	4.45	4.52	0.929 (0.79-0.98)
How the samples were selected, randomly, or was the census undertaken?	4.60	4.55	0.908 (0.76-0.97)
Was the probability of bias minimal?	4.50	4.55	0.954 (0.83-0.99)
<i>Internal validation</i>			
Was the data collected directly from the subjects?	4.48	4.52	0.952 (0.83-0.99)
Was an acceptable case definition used in the study	4.43	4.40	0.976 (0.86-1.00)
Were the used study methods to measure parameters valid and reliable	4.45	4.40	0.952 (0.83-0.99)
Was the same mode of data collection used?	4.45	4.45	1.000 (0.896-1.00)
Summary of the overall risk of the study bias	4.60	4.62	0.929 (0.79-0.98)

a panel of expert judges. The articles were evaluated for bias using a risk of bias instrument, with inter-rater agreement between two authors on eight-item structured questionnaires. Aiken's V index is formulated as follows.

$$V = S / [n * (c - 1)]$$

where, S is the sum of differences between each rater's score and the lowest score in the category, n is the number of raters, and c is the maximum score in the grading scale (Higgins *et al.* 2003). Inter-rater reliability was assessed using the Kappa Index. Two authors independently scored studies, and the average score per article was calculated. Aiken's V Index determined agreement, with scores ≥ 0.7 considered acceptable.

Data analysis: A comprehensive assessment of research standards is crucial for conducting systematic reviews and meta-analyses. Guidelines such as PRISMA enhance research quality and reliability (Moher *et al.* 2015, Shamseer *et al.* 2015). Meta-analysis amalgamates data from multiple studies to derive an overarching summary estimate (Normand *et al.* 2005). To evaluate heterogeneity among studies, various statistical tools including Cochrane's Q statistic and Higgin's I statistics were employed (Mohar *et al.* 2015). Analysis was performed using R, an open-source scripting software, by utilizing multiple packages (Patil *et al.* 2018, Krishnamurthy *et al.* 2021). Fixed and random effects models were used to accommodate variations in study outcomes. Demonstrations such as forest plots were used to depict effect sizes and confidence intervals for each study (Sushma *et al.* 2021). Heterogeneity was assessed using the I^2 statistic, and meta-regression was employed to explore potential moderators. Publication bias was evaluated using funnel plots and Egger's test (Egger *et al.* 1997). LSD prevalence was calculated using a total sample size of 4,49,873, with cattle comprising 95.2% and buffaloes 4.8%.

RESULTS AND DISCUSSION

Assessment of quality of studies: Inter-rater reliability was assessed using the Kappa statistic (Table 1), and agreement between the two authors' rating scores was measured using Aiken's V Index (Suresh *et al.* 2022). For

studies where the Aiken V Index exceeded 0.7, indicating acceptable study quality, an average score of 0.78 was calculated.

Publication bias: The funnel plot (Fig. 3) indicates some presence of publication bias, with visual inspection revealing slight asymmetry. To address this, meta-regression was employed with sample size as the risk of bias factor, resulting in non-significance ($P > 0.05$) and effectively mitigating the impact of publication bias in the study.

Meta-regression to identify the factors affecting the heterogeneity: Meta-regression revealed strong evidence of high heterogeneity among selected studies on the prevalence of LSD in livestock. To explore potential covariates that may influence the overall estimate's magnitude and direction, a univariate meta-regression analysis was performed. However, meta-regression with the Study period [regression coefficient (Q_m)=610.39, $P < 0.001$], sample size (events q_m =706.01, $P < 0.0001$), detection techniques (tests; Q_m = 614.36, $P < 0.001$), category of species (q_m =671.22, $P=0.010$) and continent (Q_m = 674.88, $P < 0.001$) suggested that the covariates had a significant effect on the heterogeneity between studies (Table 2). In conclusion, the necessity for a subgroup was determined to refine the prevalence rates of LSD, particularly concerning region-wise, diagnostic tests-wise, and species-wise variables.

Subgroup analysis: The pooled prevalence of LSD at 14% across Asia and African countries. Stratification was employed to explore LSD prevalence further, considering variables like study period, sample size, test methods, species, and continents. In the sub-group analysis, it was found that a notable divergence in LSD prevalence, with Africa reporting 21% compared to Asia's 11%. This analysis identified sources of heterogeneity, with heterogeneity coefficients of 0.03 for Africa and 0.06 for Asia. These findings strongly suggest a higher prevalence of LSD in the African continent compared to Asia. The studies conducted before 2019 showed the highest prevalence rate at 16%. whereas studies conducted after 2019 reported a slightly lower prevalence rate of 12%. This decline in prevalence rates could be attributed to

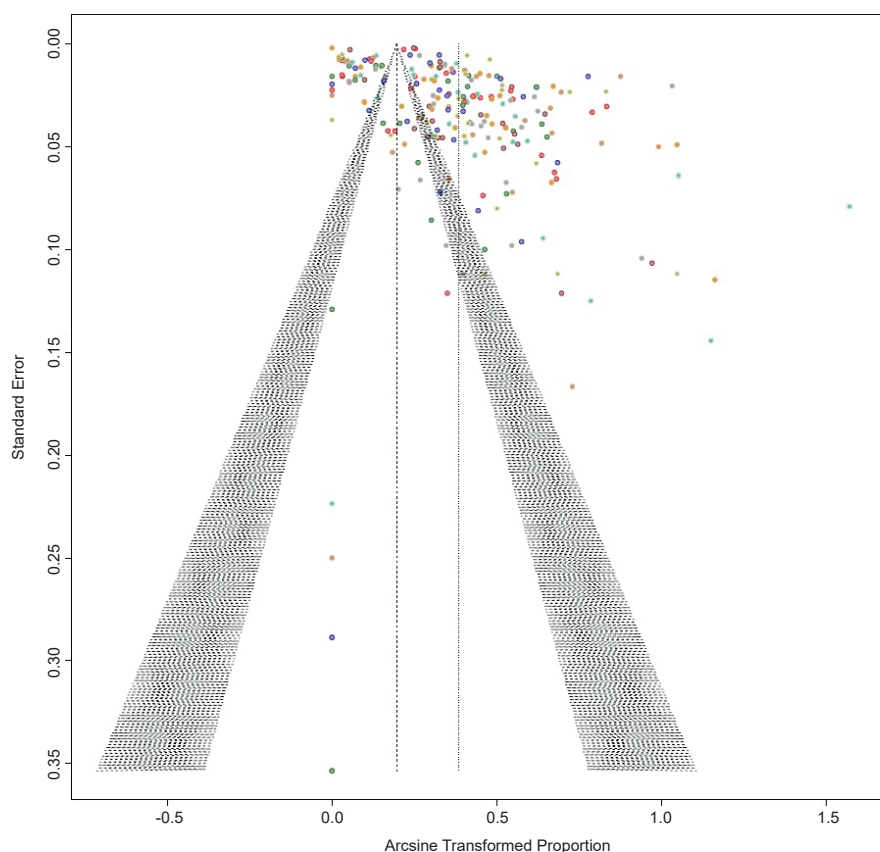


Fig 3. Funnel plot for ascertaining the occupancy of publication bias.

several factors, such as improved disease surveillance, implementation of vaccination campaigns, and enhanced control measures over time. Studies with below-median sample sizes reported the highest prevalence rate at 20%, while those with above-median sample sizes showed the lowest prevalence rate of 9%. Having studies with larger sample sizes is desirable, as they offer the reliability of the findings. The studies with smaller sample sizes also contribute valuable information, especially in areas with limited resources. It is essential to consider both types of studies in meta-analyses, as they each provide unique insights into a comprehensive understanding of LSD prevalence. Clinical observation showed a 19% prevalence followed by other tests and PCR with 12 and 13%, respectively. The studies

subjected clinical epidemiological and histopathological examinations against LSD by considering mild and severe illness due to LSD the samples detection of viral DNA by PCR test (El-Gohary *et al.* 2013). The study emphasized the PCR approach as a rapid, sensitive, and specific method for LSDV detection and disease diagnosis confirmation (Fawzi *et al.* 2022). Diagnostic tests like PCR, ELISA, and KOH deduction yielded a higher average of positive cases, suggesting that combining these test procedures can help reduce both false-negative and false-positive results. In the group of species, cattle had the highest prevalence of LSD with 15%, whereas buffaloes had merely a 1% prevalence rate. This emphasizes the significant impact of the disease on cattle populations. However, it is worth noting that LSD

Table 2. Meta-regression of epidemiological factor studies of LSD in livestock: Investigating heterogeneity and effect size

Particular		SE	Z-value	Est [95 % CI]	QM	P-value
Study period	Before 2019	0.03	14.34	0.16[0.13-0.18]	610.39	<0.0001
	After 2019	0.02	20.12	0.12[0.09-0.16]		
Sample size	Low (1)	0.02	21.86	0.9 [0.07-0.12]	706.01	<0.0001
	High (2)	0.02	15.10	0.20 [0.17-0.24]		
Detection techniques	Clinical observation	0.04	12.58	0.19[0.16-0.23]	614.36	<0.0001
	Others	0.08	4.54	0.12[0.06-0.20]		
	PCR	0.02	20.87	0.13 [0.11-0.16]		
Category of species	Buffaloes	0.07	0.97	0.01 [0.00-0.02]	671.22	<0.0001
	Cattle	0.02	25.74	0.15 [0.13-0.17]		
Continents	Africa	0.02	18.90	0.21 [0.18-0.24]	669.44	<0.0001
	Asia	0.02	17.67	0.11 [0.08-0.14]		

Table 3. Unveiling LSD stratification pattern: In-depth explanation of factor variations using sub-group analysis

Group/sub-group		I ² (%)	C ² (%)	P-value	Total no. of studies	Total no. of samples	Prevalence (%)	95% CI
Study period	Before 2019	100.00	0.04	0	36	306748	16.00	[0.13:0.18]
	After 2019	99.00	0.08	0	17	143125	12.00	[0.09:0.16]
Sample size	Low (1)	95.00	0.06	0	32	14839	20.00	[0.17:0.24]
	High (2)	100.00	0.05	0	30	435034	9.00	[0.07:0.12]
Detection techniques	Clinical observation	97.00	0.02	<0.01	7	39495	19.00	[0.16:0.23]
	Others	98.00	0.03	<0.01	4	5057	12.00	[0.06:0.20]
	PCR	99.00	0.07	0	39	405321	13.00	[0.11:0.16]
Category of species	Buffaloes	94.00	0.02	<0.01	4	21353	1.00	[0.00:0.02]
	Cattle	99.00	0.05	0	49	428520	15.00	[0.13:0.17]
Continents	Africa	99.00	0.03	0	18	92614	21.00	[0.18:0.24]
	Asia	99.00	0.06	0	31	357259	11.00	[0.08:0.14]

*Multiple surveillance results within a single study.

can also affect other ruminant species, including buffaloes and other species (Table 3).

The systematic review, and meta-analysis, on the prevalence of LSD in livestock have identified a high prevalence of LSD in cattle and buffaloes, particularly in Africa and Asia. Adopting comprehensive LSD management strategies, such as vaccination and stringent quarantine measures, using accurate and standardized diagnostic tools and surveillance systems for promptly detecting LSD cases can significantly mitigate the disease's prevalence and economic loss on the livestock industry. This understanding, in turn, can facilitate the identification of priorities in veterinary healthcare, prevention, and policy implementation. These insights are valuable for policymakers, veterinarians, and researchers, contributing to global efforts in combating LSD.

ACKNOWLEDGEMENTS

The authors wish to thank Dikshita T. Young Professional and others from NADCP, NADREs, DBT-One-Health of spatial epidemiological lab, ICAR-NIVEDI for providing the necessary facilities for carrying out this work.

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