

Review Article

One Health Bulletin

Trends and evolution of research on *Phlebotomus argentipes*, a potential vector of visceral leishmaniasis

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ABSTRACT

Neglected tropical disease, visceral leishmaniasis is a significant health issue globally, caused by *Leishmania donovani*, a protozoan parasite, transmitted by an insect vector sandfly *Phlebotomus (P). argentipes*. Understanding the disease transmission dynamics is crucial, with *P. argentipes* being the primary vector in the Indian subcontinent. The study utilized citation network analysis (CNA) to investigate the scientific literature on the sandfly species *P. argentipes*, focusing on the distribution of publications over the past 80 years. A total of 2 601 publications were initially retrieved, refined through manual screening to 400 relevant articles published by 1 209 authors in 150 journals in the last eight decades. Data included publication details, such as association of authors, citations, journals, and affiliations. CNA involved the use of VOSviewer software for creating bibliographic networks, visualizing and analyzing citation networks. Core publications highlighted key research areas, including vector control, taxonomy, genetics, and epidemiology. Collaboration across countries and disciplines was evident, emphasizing the global effort to combat visceral leishmaniasis. By analyzing extensive publication data, CNA revealed key research clusters and the most cited works, showing that research into visceral leishmaniasis transmission and vector control has intensified since the 2000s, with significant contributions from India which is highly endemic for visceral leishmaniasis followed by USA, and the UK.

KEYWORDS: Citation network analysis; Kala-Azar; *Leishmania donovani*; *Phlebotomus argentipes*; Sandfly; Visceral leishmaniasis

1. Introduction

Leishmaniasis, a neglected tropical disease caused by protozoan parasites of the genus *Leishmania*, poses a significant health burden in many parts of the world. There are three main forms of the leishmaniasis: the most common cutaneous leishmaniasis (CL), the most severe visceral leishmaniasis (VL) also known as Kala-azar, and the most disabling form mucocutaneous leishmaniasis[1]. In East Africa and South-East Asia including India, complication of VL in the form of PKDL (Post-Kala-azar Dermal Leishmaniasis) diagnosed by hypo-pigmented flat skin (macular) rash, combined with slightly elevated nodular rash also observed in some cases[2,3]. Co-infection of HIV (human immunodeficiency virus) and *Leishmania* has been reported from many countries with majority of cases from Brazil[4], Ethiopia[5] and India[6]. People infected with HIV have very high chances of developing the kala-azar disease than others in the endemic areas[7].

Leishmania (L.) donovani, the pathogenic agent of VL was discovered in 1903 but it took more than 40 years to discover the

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vector that transmit the disease[8]. VL is transmitted primarily through the bites of an infected sandfly though the principal vector varies, depending on the geographical location[9,10]. Understanding the vector responsible for transmitting Kala-azar is crucial for developing effective control strategies to mitigate its impact on public health[11]. In the Indian subcontinent, *Phlebotomus (P.) argentipes*, serves as the primary vector. The lifecycle of *P. argentipes* is intricately linked with the transmission cycle of *Leishmania* parasites (Figure 1)[12,13]. *P. argentipes* is primarily found in the Indian subcontinent, and countries like Bangladesh, Nepal and Sri Lanka. The presence of sibling species complex in *P. argentipes* reassessed due to morphological, behavioral, and distributional variations[14]. The natural infections of *P. argentipes* populations with *L. donovani* in the epidemiologically active zones of Kerala incriminated this species as the vector of both VL and atypical CL[15–17]. Environmental and climatic changes have a substantial impact on the distribution and behavior of *P. argentipes* and, consequently, the transmission dynamics of VL and CL in India. Rising temperatures, changes in rainfall patterns, and increased humidity levels provide favorable conditions for sandfly populations, potentially expanding their range into new areas[18]. Insecticide resistance is another challenge in controlling *P. argentipes* populations. Resistance to commonly used insecticides has been reported in sandfly populations across India, which undermines the effectiveness of vector control measures such as indoor residual spray (IRS)[19]. A vast body of literature has been published on various aspects of *P. argentipes* as a potential vector of VL, highlighting its importance in the transmission of *L. donovani*. Citation network analysis (CNA) of this literature provides valuable insights into the evolution of research trends focused on the species, its ecological preferences, and its role in disease transmission. By examining the interconnectedness of studies, researchers can better understand how knowledge about *P. argentipes* has progressed, as well as the diverse factors influencing its distribution, behavior, and vector competence.

2. Methods

2.1. Data source

The data was retrieved using the Web of Science database with intended keywords like "*Phlebotomus argentipes*", "VL vector", "Kala-azar vector" and "Phlebotominae" (Figure 2). Article spanning from 1942 (the year of discovering the vector for VL) to March 2024 were retrieved for analysis. Web of Science also facilitates to add references to the library from external databases

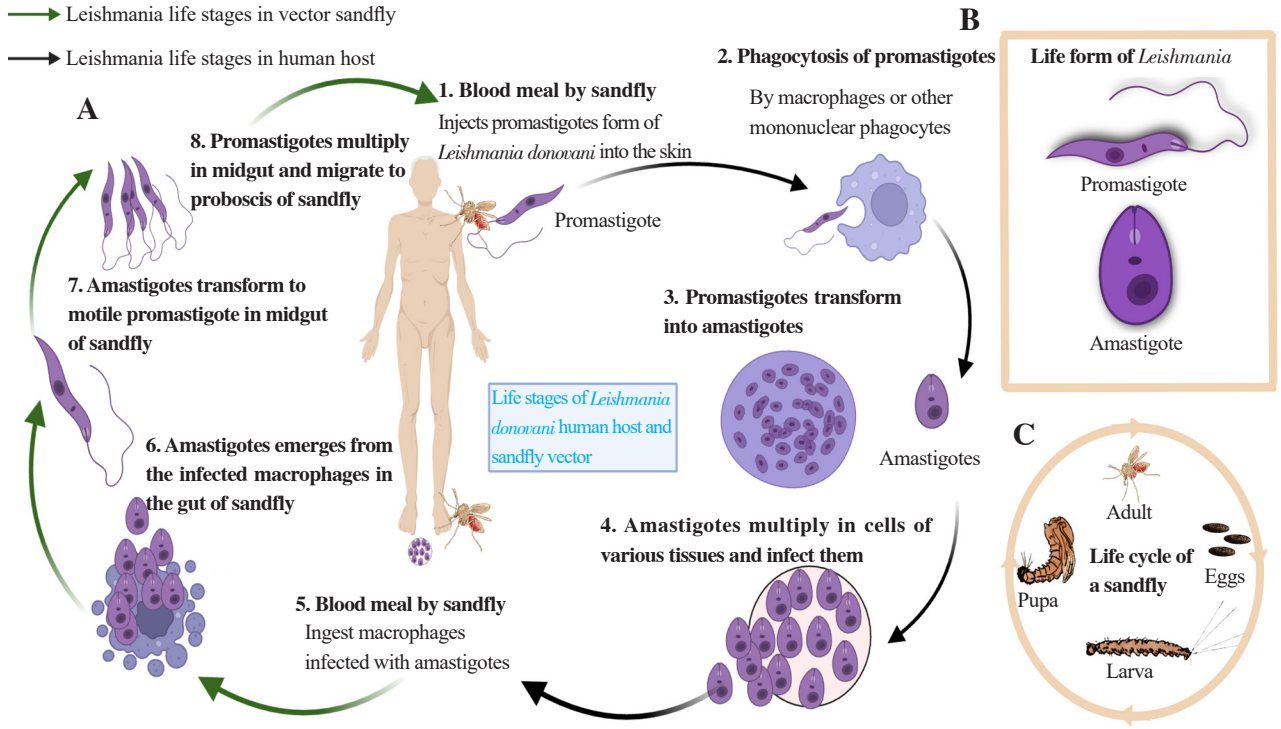


Figure 1. Transmission cycle (A) of *Leishmania donovani* in humans, promastigote and amastigote forms (B) of *Leishmania*, and life stages (C) of sandfly *Phlebotomus argentipes*[12,13].

including Science Citation Index Expanded (SCI-EXPANDED), Book Citation Index – Social Sciences & Humanities (BKCI-SSH), Book Citation Index – Science (BKCI-S), Current Chemical Reactions (CCR-EXPANDED), Emerging Sources Citation Index (ESCI), Index Chemicus (IC), Conference Proceedings Citation Index – Science (CPCI-S) and Social Sciences Citation Index (SSCI).

After preliminary analysis, 2 601 publications including books, chapters, conference proceedings, reviews *etc*. were curated. Articles which were not relevant to research on vectorial competency of *P. argentipes* were excluded after manual screening, including the retraction articles. A total of 400 articles contributed by 1 209 authors were finally saved in the master list for consideration that specifically published on the topic sharing the wide research areas from taxonomy, molecular biology, vector incrimination, ecology and insecticide susceptibility of *P. argentipes*. The downloaded data from Web of Science database having information regarding year of publication, authors, co-authors, citations, journals, publishers, affiliation of authors, institutions, funding, languages and geographical distribution.

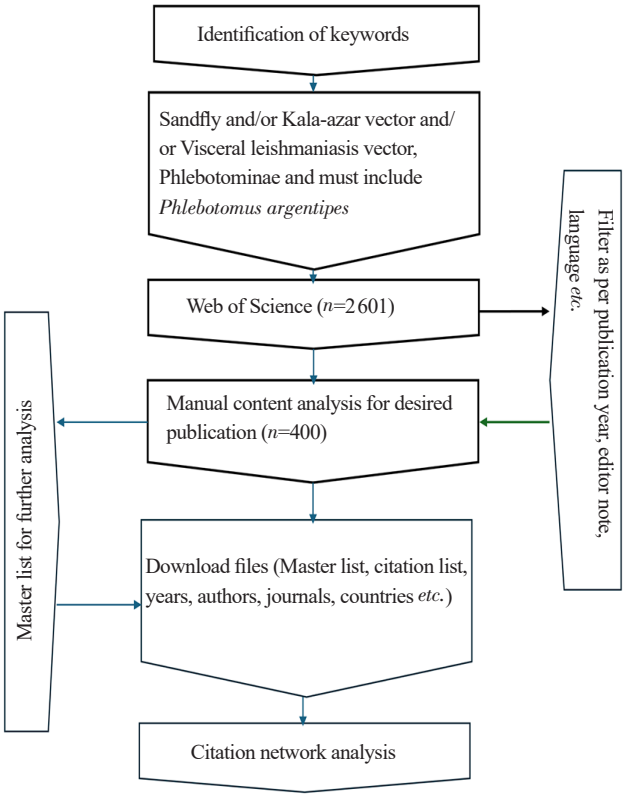


Figure 2. Literature screening and citation network analysis.

2.2. Network data analysis

VOSviewer software was used for analysis, which allows the visualizations and analysis of the citation network of research publications by facilitating further downloads of citation network of thousands of publications directly from Web of Science. Thus, a citation network is composed of millions of interconnected publications and their citations. The most mentioned publications were quantitatively analysed using the attribute citation score which include not only the connections within Web of Science, but many external connections were also quantified by using the equation given below[20].

$$V(C_1, ..., C_n) = \sum_{i<j} \delta(C_i, C_j)(S_{ij} - \gamma)$$

Where "*n*" represents the number of publications included in the visualization of the citation network. Each publication corresponds to a node in the citation network; "$C_{i/j}$" denotes the closeness of publications i and j in the citation network; "S_{ij}" represents the weight of the repulsive force between publications i and j; "γ" represents the exponent of the repulsive force.

The clustering functionality was applied to assign a group to related publications. As a result, based on the citation network the most related publications were grouped together. Core publication functionality was used to identify the core publications to segregate them from irrelevant ones. The publications having at least one citation were considered to build the network of core publications. The subgroups of co-authorship, keyword occurrence, bibliographic coupling or co-citation maps were created by using the bibliographic data. CNA technique used in analysis of scientific literature relevant to a concept, topic or a theme. It helps in quantitative and qualitative analysis of relevant additional publications to the concept and builds a network of subgroups based on associated authors, their research, citations and co-citations[21]. CNA makes it possible to analyse the relationship between research groups and their publications on related scientific concept using the VOSviewer software[20]. This study explored the research publications from the last 80 years on *P. argentipes* as a vector and analysed through citation network analysis. Comparatively to traditional review, CNA provides an exhaustive quantitative data by making groups and subgroups of closely related research work within the main theme including the details of publications, citations, co-citations, authors, co-authors, countries and journals publishing the similar research[22–23].

3. Results

VL or Kala-azar first came to the attention of Western world in 1824 in Jessore (now Bangladesh), had a devastating epidemic[24].

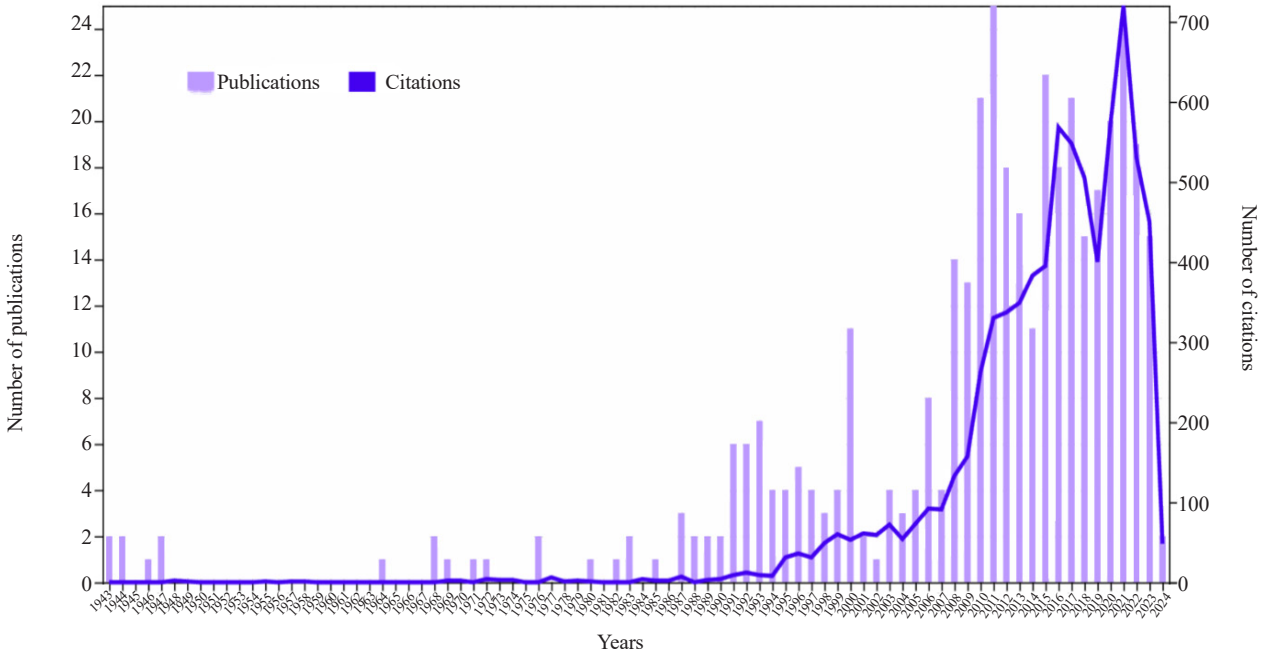


Figure 3. Number of articles and citations per year.

After identification of the pathogenic agent, *L. donovani* in 1903 by William Leishman and Charles Donovan independently, L. Rogers worked on cultures of this parasite in 1904, and it became probable that a hematophagous arthropod was responsible for transmission of the disease[8]. Thomas Nelson Annandale and Enrico Adelelmo Brunetti discovered the sandfly, *P. argentipes* in 1908[25]. In 1942, a team led by H.E. Shortt successfully transmitted *L. donovani* to five human volunteers through the bites of colonized *P. argentipes*, and the race was over to discover the vector of VL[8,26]. Then the race was started to research out every possible aspect of *P. argentipes* to eliminate the VL as public health problem. The first article appeared in search database after the discovery of *P. argentipes* as potential vector of Kala-azar was published by Conybeare on transmission of Kala-azar by the sandfly in British Medical Journal[27]. Totally 1 209 authors and co-authors from 60 countries published the 400 articles. The majority of the articles (78.5%) were research articles, while 8.5% were review articles. The remaining publications included conference proceedings, book chapters, and data papers. Additionally, 98.5% of the publications were in English, with the remainder in French, German, Portuguese, and Turkish, all of which included English titles and abstracts.

3.1. Publication trends

The data retrieved, shared the publications from 20th to 21st century. The articles published in 20th century count for 18% in 57 years while the 21st century count for 82% in 24 years, although no article appeared in database from 1948 to 1964 relevant to the theme. There was steep increase in publications from 2008, the highest number of publications were recorded in 2011 (6.25% of the total published articles) but highest number of citations were recorded in 2021 (Figure 3).

3.2. Most cited publications

Table 1 highlights the top 10 research articles with highest citations including three review articles and seven research articles addressing the ecology, physiology, molecular biology, insecticide susceptibility, immunology, genetics, taxonomy of the sandfly and the epidemiology of the Kala-azar. The most cited review work published by Alexander and Maroli with 214 citation on “Control of phlebotomine sand flies”[28].

In CNA, publications with similar co-citations were assigned to a single group, creating a cluster of closely connected publications through their co-citations. Each of this group represented a different research area but connected to other groups that shared the same cited articles. To differentiate from other such groups, these were assigned to different colours. Each circle in a same group with similar colour depicts a publication, the size of the circle corresponds to the number of co-citations. The bigger the circle, the greater number of co-citations (Figure 4A). Analysis of co-citations with cited references produced 1 632 cited references with minimum number of 1 citation of a cited reference but by default only 1 000 can be analysed in software that grouped the publications in 11 clusters with 46 066 links and a total strength

Table 1. Top ten cited articles.

Authors	Title	Source title	Year	Citations
Alexander B, Maroli M[28]	Control of phlebotomine sand flies	Medical and Veterinary Entomology	2003	214
Feliciangeli MD[29]	Natural breeding places of phlebotomine sand flies	Medical and Veterinary Entomology	2004	180
Bora D[12]	Epidemiology of visceral leishmaniasis in India	National Medical Journal of India	1999	180
Pimenta PFP, Saraiva EMB, Rowton E, Modi GB, Garraway La, Beverley SM, *et al.*[30]	Evidence that the vectorial competence of phlebotomine sand flies for different species of *Leishmania* is controlled by structural polymorphisms in the surface lipophosphoglycan	Proceedings of the National Academy of Sciences of The United States of America	1994	162
Anderson JM, Oliveira F, Kamhawi S, Mans BJ, Reynoso D, Seitz AE, *et al.*[31]	Comparative salivary gland transcriptomics of sand fly vectors of visceral leishmaniasis	BMC Genomics	2006	119
Addy M, Nandy A[32]	Ten years of Kala-azar in West-Bengal Part Ⅰ. Did post-Kala-azar dermal leishmaniasis initiate the outbreak in 24-Parganas?	Bulletin of the World Health Organization	1992	105
Joshi PB, Sacks DL, Modi G, McMaster WR[33]	Targeted gene deletion of *Leishmania* major genes encoding developmental stage-specific leishmanolysin (GP63)	Molecular Microbiology	1998	97
Bern Caryn, Courtenay Orin, Alvar Jorge[34]	Of cattle, sand flies and men: A systematic review of risk factor analyses for South Asian visceral leishmaniasis and implications for elimination	PLOS Neglected Tropical Diseases	2010	94
Dionisio D, Esperti F, Vivarelli A, Valassina M[35]	Epidemiological, clinical and laboratory aspects of sand fly fever	Current Opinion in Infectious Diseases	2003	91
Novella IS, Clarke DK, Quer J, Duarte EA, Lee CH, Weaver SC, *et al.*[36]	Extreme fitness differences in mammalian and insect hosts after continuous replication of vesicular stomatitis-virus in sand fly cells	Journal of Virology	1995	91

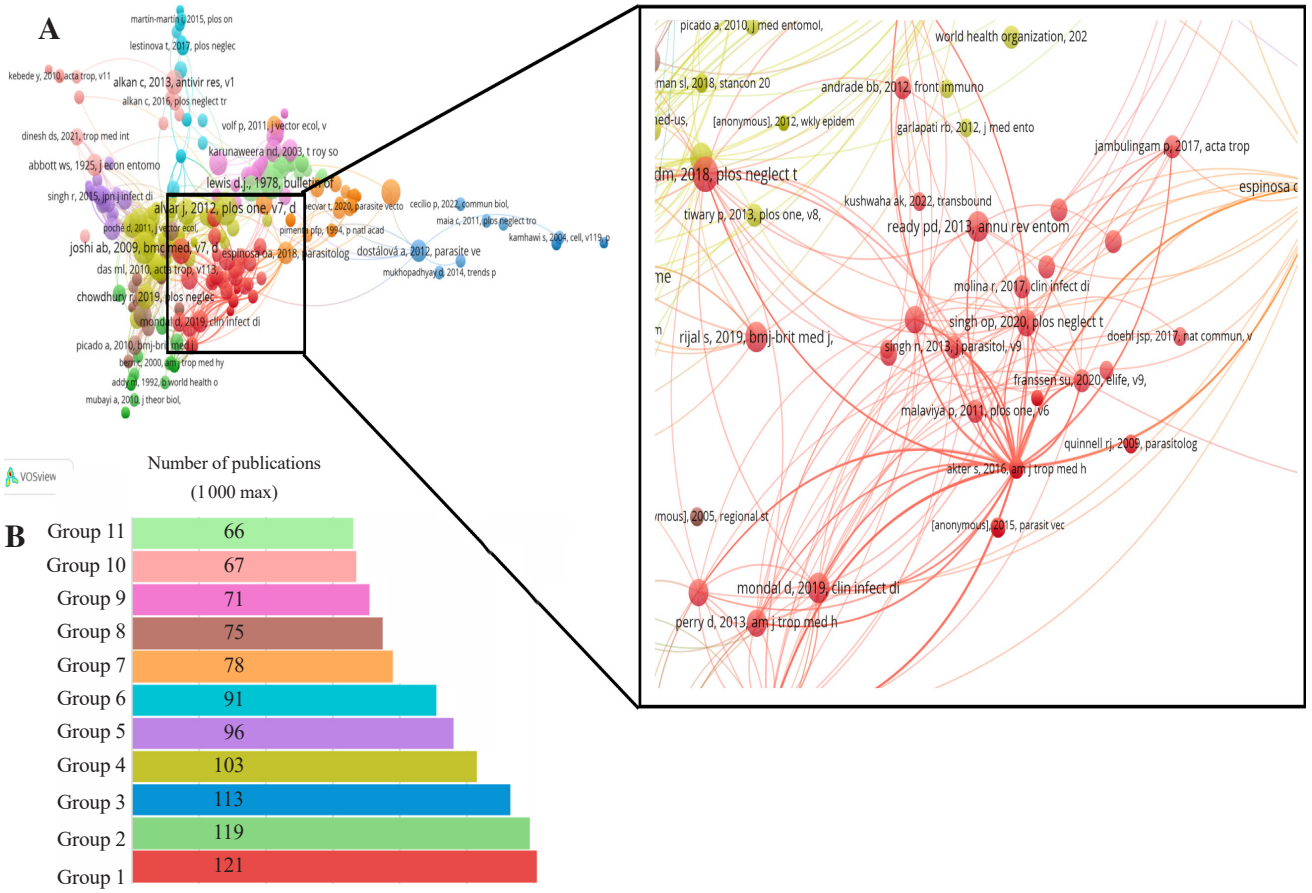


Figure 4. Cluster analysis of co-citations: (A) Citation network of the shared co-citations among authors with inset: Enlarged view of a group network; (B) Grouping of publications with shared co-citations.

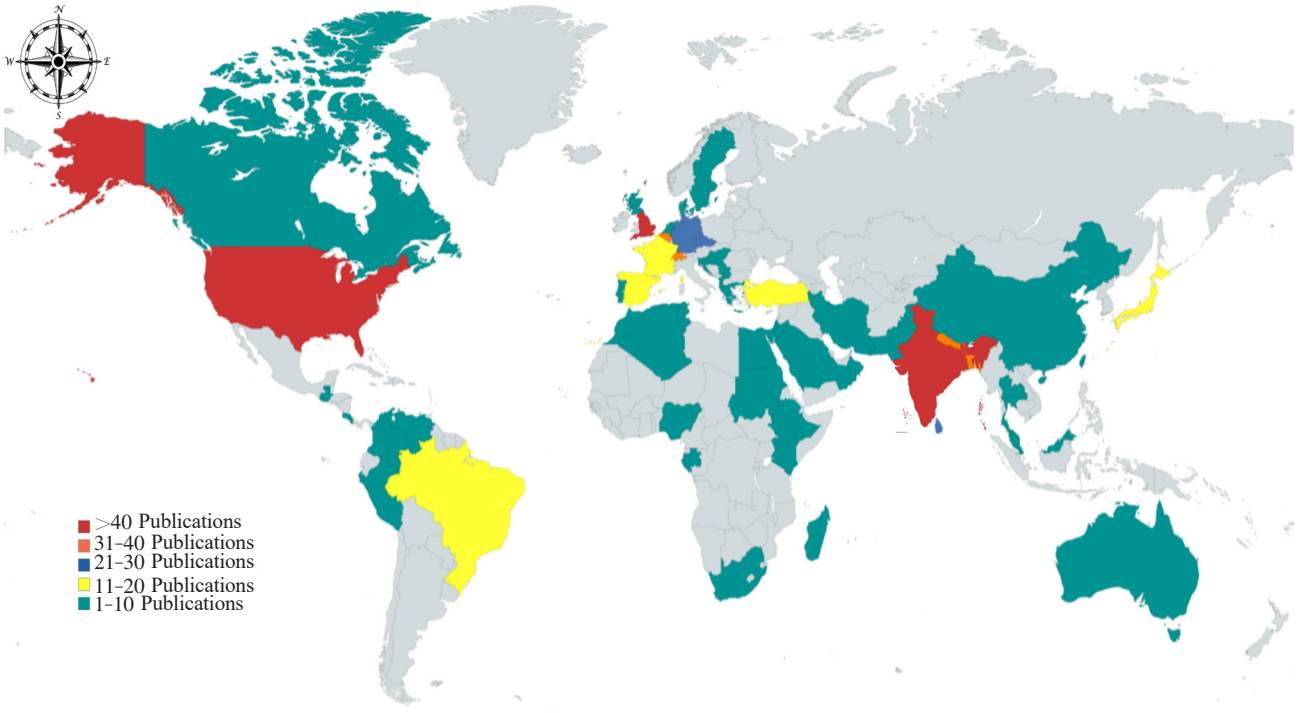


Figure 5. Publications published by different countries.

of 47 777 (Figure 4B). These clusters were associated with each other through co-citations. Publications from authors like Joshi, Alvar, Lewis, and others having maximum number of co-citations. The group (red) for example have 121 co-citations out of the 1 000 analysed, the various circle in this groups were publications with closely related topics (Figure 4A).

3.3. Publication by countries

The 400 publications were contributed by sixty countries across the world but 22 record(s) (5.5%) do not contain data. About 65.0% of the publications were published by the most endemic countries for VL like India (40.8%), Nepal (9.0%), Bangladesh (8.3%) and Sri Lanka (6.5%). India published 40.8% of the publication, England (16.3%) followed by USA (16.0%) (Figure 5).

3.4. Publications by journals

Co-citation analysis with cited sources analysed 602 resources among 150 journals, one of which was not connected to any source. The total strength of the co-citation links with remaining 601 resources was calculated and grouped into 18 cluster groups with different colours (Figure 6). The maximum number of co-citations shared by the journals of group one with 87 resources. *PLoS Neglected Tropical Disease* and *American Journal of Tropical Medicine and Hygiene* in group 8 and *Parasite & Vectors* in group 5 have maximum number of publications but shared lesser co-citations with other sources of publications.

PLoS Neglected Tropical Disease published the highest number of articles (35/400, 8.8%) followed by *Parasites & Vectors* (20/400, 5.0%) and *American Journal of Tropical Medicine and Hygiene* (20/400, 5.0%). Interestingly, *Medical and Veterinary Entomology* published twenty articles including the highly cited one (Table 1) and occupied 2nd position among highly cited journals while *National Medical Journal of India* stood at 10th position by publishing only two articles (Figure 7).

The co-occurrence analysis on the keywords from titles and abstracts of the publications with minimum number of ten occurrences produced 1 954 items out of which 41 meet the threshold. The text items/keywords in publications clustered into three main groups. Group 1 (Red) includes publications on the presence and absence of the parasite and vector in the host. The cited studies on species of *Leishmania* and sandflies are grouped in this cluster. Group 2 (Green) includes publications on the effects of insecticides, efficacy, interventions, and IRS on the sandfly vector. Group 3 (Blue) focuses on insecticides such as DDT and deltamethrin, as well as their resistance in the vector (Figure 8).

4. Discussion

Leishmaniasis, particularly VL, continues to be a significant global health issue, especially in endemic regions of East Africa and Southeast Asia. The disease, caused by *Leishmania* parasites and transmitted by the *P. argentipes* sandfly, leads to severe health consequences.

CNA of the scientific literature provides valuable insights into the trends, patterns, and collaborations that have shaped research on potential vector *P. argentipes*. By analyzing extensive publication data, CNA revealed key research clusters and the

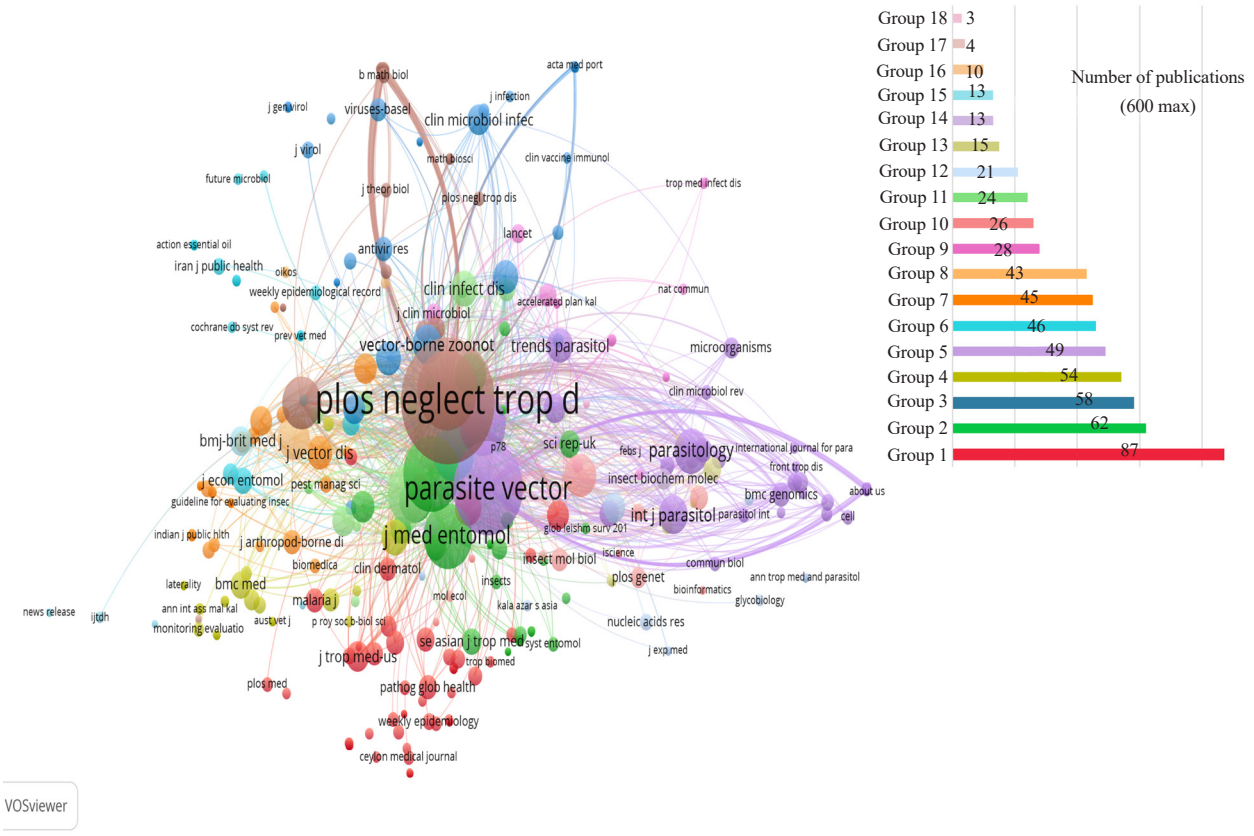


Figure 6. Co-citation network analysis of sources.

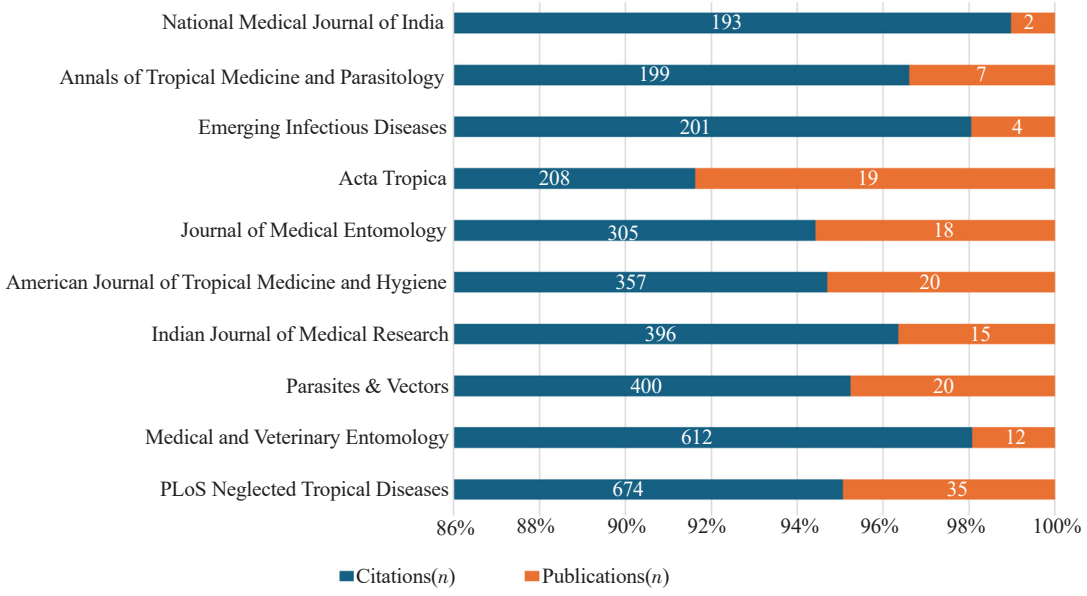


Figure 7. Top 10 journals with citations and number of publications.

most cited works, showing that research into VL transmission and vector control has intensified since the 2000s, with significant contributions from India which is highly endemic for VL followed by USA, and the UK. Highly cited publications in citation network analysis of *P. argentipes* serve as markers of influential research, guiding the direction of future studies, shaping policies, and enhancing the development of effective vector control strategies. These papers help define the scientific landscape of *P. argentipes* research and its role in the transmission of VL. The journals played the key role in publishing the articles. *PLoS Neglected Tropical Disease*, *American Journal of Tropical Medicine and Hygiene*, and *Parasites & Vectors* published the 18.8% of the articles among 150 journals. Significance of journals in CNA helps in understanding the dissemination of knowledge, identifying leading research

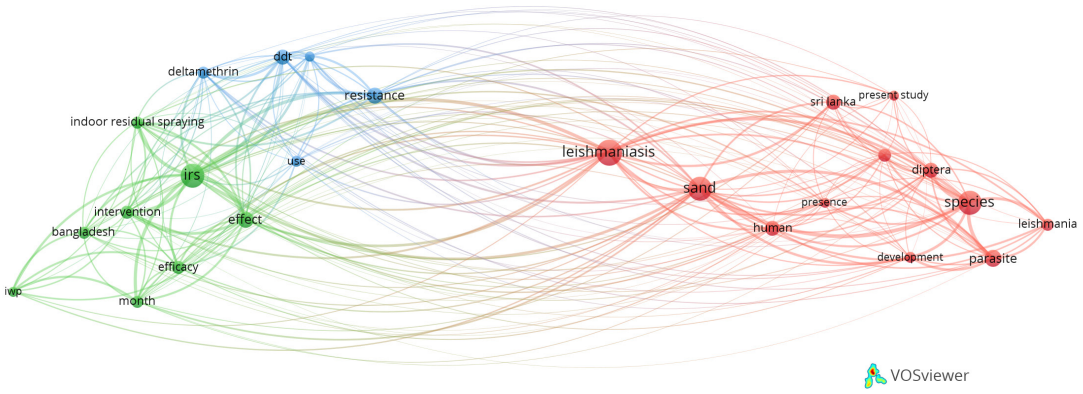


Figure 8. Cluster analysis of publications with text item keywords.

platforms, tracking global and regional trends, and promoting high-quality research. Analyzing publications by countries provides essential insights into the global landscape of research on this vector. It helps in understanding regional research priorities, fostering international collaboration, identifying emerging trends, and assessing the impact of local research on global disease control efforts. The identification of emerging research areas, such as insecticide resistance and vector ecology, highlights the evolving nature of the field and the critical need for continued innovation. This research provides a more comprehensive understanding of the factors influencing VL transmission, enabling better-targeted interventions and policies. The ability to track and analyze citation networks enhances collaboration among global research teams and fosters the exchange of knowledge, essential for tackling a disease that, while preventable and treatable, still affects millions globally.

5. Conclusions

The study offers a unique and objective review analysis of the core research articles published on *P. argentipes*, a potential vector of VL or Kala-azar. Discovering the taxonomy, life cycle, vectorial competencies, genetics, molecular, host-vector-parasite relation and its elimination by using various IRS techniques to overcome the burden of visceral leishmaniasis as a public health problem. In addition, the CNA provides a thorough analysis of hundreds of publications published on the theme from past 80 years using the Web of Science database explored with VOSviewer. The data analysis from the 20th and 21st century provides a clear insight on the focus and priority areas of the research. Co-citation analysis clearly indicated the closely related research by the scattered scientist communities from different countries across the world. The endemicity of the visceral leishmaniasis in countries like India, Sri Lanka and Bangladesh also resulted in more research and publications. Moreover, the study provides a clear idea about the journal and publishers publishing the neglected tropical disease research.

Conflict of interest statement

The authors claim there is no conflict of interest.

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Data availability statement

The data supporting the findings of this study are available from the corresponding author upon request.

Authors' contributions

Sharma YP conceptualized, interpreted, and analyzed the data, and developed the graphics. Sindhania A curated and analyzed the data. Kumar A and Kumar A contributed to writing and reviewing the manuscript. All authors read and approved the final manuscript.

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