



Research article

Mapping knowledge landscapes and emerging trends of Marburg virus: A text-mining study

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ABSTRACT

Background: Marburg virus (MARV), a close relative of Ebola virus, could induce hemorrhagic fevers in humans with high mortality rate. In recent years, increasing attention has been paid to this highly lethal virus due to sporadic outbreaks observed in various African nations. This bibliometric analysis endeavors to elucidate the trends, dynamics, and focal points of knowledge that have delineated the landscape of research concerning MARV.

Methods: Relevant literature on MARV from 1968 to 2023 was extracted from the Web of Science Core Collection database. Following this, the data underwent bibliometric analysis and visualization procedures utilizing online analysis platform, CiteSpace 6.2R6, and VOSviewer 1.6.20. Three different types of bibliometric indicators including quantitative indicator, qualitative indicators, and structural indicators were used to gauge a researcher's productivity, assess the quality of their work, and analyze publication relationships, respectively.

Results: MARV is mainly prevalent in Africa. And approximately 643 confirmed cases have been described in the literature to date, and mortality observed was 81.2 % in overall patients. A total of 1014 papers comprising 869 articles and 145 reviews were included. The annual publications showed an increasing growth pattern from 1968 to 2023 ($R^2 = 0.8838$). The United States stands at the forefront of this discipline, having dedicated substantial financial and human resources to scientific inquiry. However, co-authorship analysis showed the international research collaboration needs to be further strengthened. Based on reference and keywords analysis, contemporary MARV research encompasses pivotal areas: primarily, prioritizing the creation of prophylactic vaccines to impede viral spread, and secondarily, exploring targeted antiviral strategies, including small-molecule antivirals or MARV-specific monoclonal antibodies. Additionally, a comprehensive grasp of viral transmission, transcription, and replication mechanisms remains a central focus in ongoing investigations. And future MARV studies are expected to focus on evaluating clinical trial safety and efficacy, developing inhibitors to contain viral spread, exploring vaccine immunogenicity, virus-host association studies, and elucidating the role of neutralizing antibodies in MARV treatment.

Conclusion: The present study offered comprehensive insights into the contemporary status and trajectories of MARV over the past decades. This enables researchers to discern novel

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collaborative prospects, institutional partnerships, emerging topics, and research forefronts within this domain.

1. Introduction

The Marburg virus (MARV) is the pathogen responsible for causing Marburg disease (MARD) in humans, with a fatality rate that could reach as high as 90 % [1]. Belonging to the Filoviridae family, MARV genus, along with the Ebola virus genus, constitutes the two primary members of this viral family. Its transmission primarily involves zoonotic spread, often through bodily fluids. This enveloped, single-stranded negative-sense RNA virus exhibits a branched or coiled structure under electron microscopy, with a genome RNA length of approximately 19 kb, comprising seven open reading frames [2,3]. The primary pathogenic mechanisms include direct cellular damage upon host cell infection and indirect cell impairment due to the interaction between the virus and the host's immune system [4–6].

In 1967, this virus was transmitted from infected monkeys in Uganda to Europe, and it was first identified in Marburg, Frankfurt, and Belgrade [7]. Despite few early reported cases of MARV in Africa, it did not garner sufficient attention. It was not until the Ebola virus disease (EVD) outbreak in West Africa in 2014 that MARV, alongside EVD, attracted global attention [8,9]. The World Health Organization (WHO) designated it as a priority infectious disease with the potential for a major outbreak in 2015 and listed it as a priority emergency disease in 2018, which spurred the formulation of MARV control measures and the development of diagnostic products [10,11]. The most recent MARV outbreak occurred in February 2023 in Equatorial Guinea and neighboring countries [12]. Following the outbreak, WHO held emergency meetings. Expert teams were dispatched to Equatorial Guinea and surrounding regions, preparing to promptly detect, isolate, and care for individuals possibly infected with the Marburg virus. Equatorial Guinea and Tanzania respectively declared the end of the epidemic on June 2nd and June 8th after 42 days with two consecutive negative laboratory test results (the two longest incubation periods) [13]. However, despite the declared end, unidentified transmission chains persist, signaling a global need for vigilance in disease prevention and control. Yet, there are currently no reliable vaccines or effective treatments for this highly contagious and lethal virus [2,3,14]. Given the potential of MARV to cause large-scale outbreaks, summarizing its global research status and trends becomes pivotal. This not only aids in deepening our understanding of the virus itself but also emphasizes the necessity for international collaboration and information sharing. Collaboration among nations and the sharing of data, technologies, and resources are crucial for expediting vaccine development and the establishment of effective control strategies in the field of MARV research. Notably, while systematic reviews or meta-analyses can offer the latest research advancements in MARV from a particular perspective, they may fall short in providing a quantitative summary of global collaborative analyses and key topics of research interest. In recent years, bibliometric analysis has gained increasing attention as a research method and could complement the limitations of systematic reviews and meta-analyses [15,16].

Bibliometric analysis, a multidisciplinary field merging mathematical, statistical, and bibliographic methods, facilitates the quantification and visualization of research trends [17]. It has become a crucial tool for assessing the quality and impact of academic works. This approach identifies and measures critical indicators of scholarly research output, citations, and influence, providing an objective and systematic evaluation framework for the academic community [18,19]. Furthermore, bibliometric analysis not only unveils the quantity and quality of academic works but also aids in identifying emerging research areas and hot topics. By visualizing data, creating scientific graphs, and constructing scientific models, it enables researchers to intuitively grasp the developmental trajectory of academia and make data-driven decisions [20]. For instance, in the field of infectious diseases, the global COVID-19 pandemic triggered by the novel coronavirus in 2019 became a pivotal research subject in the biomedical domain. A substantial amount of bibliometric analysis has summarized various aspects of COVID-19, including its pathogenesis, vaccine development, and prognosis [21–26]. However, we note the scarcity of scholarly literature conducting bibliometric analyses in the domains of the Marburg virus or Ebola virus [27,28]. Hence, this study aims to employ bibliometric methods, collecting relevant literature on the Marburg virus, to comprehensively outline the developmental trends, principal contributors, and forefront issues in this domain. More specifically, this bibliometric study aims to answer the following questions:

Question one: Derived from extant literature, what delineates the prevailing global trajectory within this domain?

Question two: Which periodicals enjoy preeminence for disseminating manuscripts within this domain?

Question three: Which nations/regions, establishments, and scholars manifest as preeminent and consequential in this domain?

Question four: What pivotal trajectories and focal points constitute the primary research pursuits? How have they evolved?

Question five: What signify the paramount research frontiers and probable focal points in the proximate horizon?

2. Methods

2.1. Data source

This study utilized Science Citation Index Expanded (SCIE) of the Web of Science Core Collection (WoSCC) database as its primary data repository. In a bid to minimize potential systematic biases stemming from database updates, a thorough and comprehensive search and screening of publications were undertaken, culminating on December 24, 2023. Previous studies have demonstrated the advantages of WoSCC database in bibliometric analysis when compared to PubMed and Scopus [29,30]. Firstly, the literature within WoSCC undergoes rigorous scrutiny, encompassing high-quality, peer-reviewed scholarly journals and publications. Secondly, WoSCC

offers comprehensive citation data and literature details, enabling researchers to conduct in-depth literature analysis and construct citation networks. Lastly, WoSCC possesses advanced search and filtering functionalities, allowing users to precisely filter and categorize search results according to specific requirements [31,32]. The aforementioned strengths of the WoSCC database render it one of the most favored databases for conducting bibliometric analysis.

2.2. Data retrieval

After an extensive review of literature and consultations with experts, we arrived at the definitive search terms, employing a strategy that encompassed title (TI), abstract (AB), and author-provided keywords (AK) for refinement. The specific search terms were as follows: Marburg virus* or Marburgvirus* or Marburg disease* or Marburg infecti* or Marburg hemorrhagic fever or Marburg hemorrhagic fever. Incorporating an extensive array of data sources necessitated the utilization of a wildcard symbol “*”, thereby accommodating varied keyword endings. For instance, the term “Marburg disease*” encompassed both “Marburg disease” and “Marburg diseases” ensuring a comprehensive coverage within the search scope. The publication timeline encompassed a 56-year period, commencing on January 1, 1968, and concluding on December 24, 2023. The selected articles for this analysis are distinctly categorized as either Article or Review Article, authored in the English language. Following the elimination of duplicate entries, a preliminary screening was conducted on the titles and abstracts of all retrieved papers, leading to the exclusion of studies deemed irrelevant to the research topic. The detailed screening procedure was illustrated in Fig. 1.

2.3. Data collection

Bibliometric indicators are categorized into three types: quantitative indicators, which gauge a researcher’s productivity; qualitative indicators, which assess the quality of their work; and structural indicators, which analyze publication relationships, including authors and countries. Therefore, all eligible literature records adhering to the outlined criteria were obtained and exported in plain text or tab-delimited file formats, encompassing a comprehensive “full record and cited references” content approach. This encompassed various details including titles, keywords, citation counts, publication dates, geographical origins, authors, affiliations, academic journal sources, impact factors (IF), H-index, funding sources, and other pertinent indicators. Among these indicators, the journal IF were extracted from the 2023 Journal Citation Report (JCR) accessible via <https://jcr.clarivate.com/>. The H-index signifies authors who have published a minimum of H papers, each receiving at least H citations [33]. The initial literature exploration, screening, and collection were carried out independently by the first two authors. After the removal of controversial issues, these records were subsequently utilized for visualization and comprehensive bibliometric analysis.

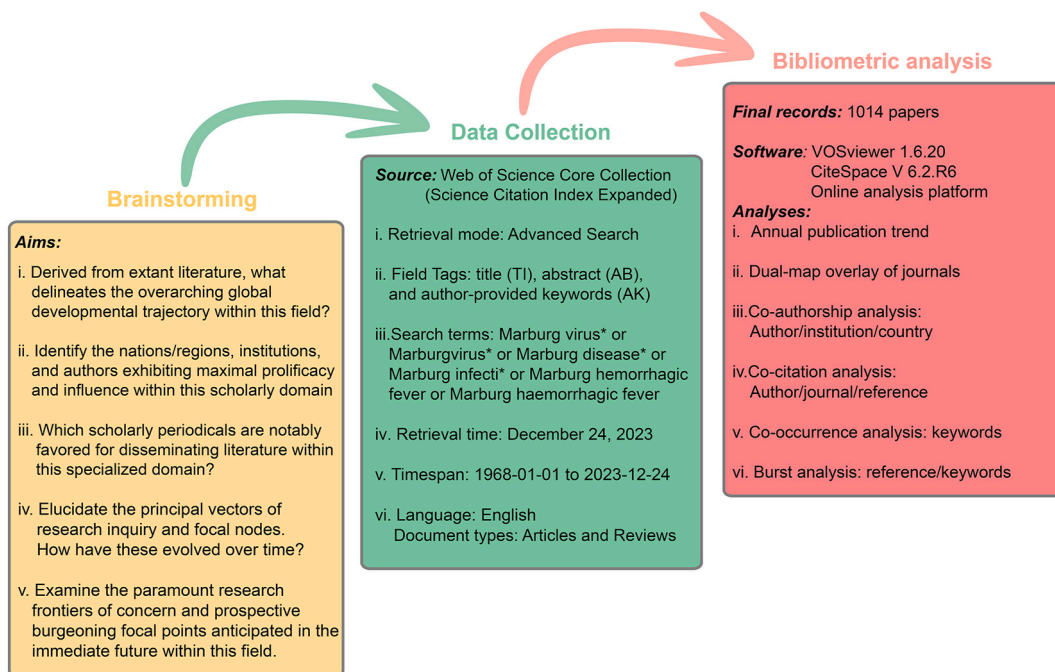


Fig. 1. The workflow of literature screening and selection.

2.4. Data analysis

2.4.1. Statistical analysis

This study primarily employed descriptive analysis as its statistical methodology. Data analysis, chart plotting, and curve fitting were performed using Microsoft Excel 2019 and R (v4.1.0). Microsoft Excel 2019 facilitated curve fitting of annual publication and citation counts. The selection of the optimal fitting model relied on achieving the highest determination coefficient (R^2).

2.4.2. Bibliometric analysis

This investigation employed science mapping methodologies encompassing citation analysis, co-authorship analysis, co-citation analysis, and keyword co-occurrence analysis. Citation analysis operates under the premise that citations serve as connections among publications, unveiling influential works within a research domain. Co-authorship analysis delves into author interactions and affiliations, outlining the social framework influencing the field's evolution. Co-citation analysis, on the other hand, presumes that publications frequently cited in tandem share thematic similarities, unveiling the intellectual framework and thematic underpinnings of a research area. Keyword co-occurrence analysis identifies thematic relationships among frequently occurring terms, unveiling topical themes and aiding in predicting future research directions. Employing these methods alongside network analysis helps delineate the structural landscape of the research domain. In addition, this study utilized a spectrum of tools and software for bibliometric analysis. The online analysis platform (<https://bibliometric.com/>), CiteSpace (version 6.2R6) [34], and VOSviewer (version

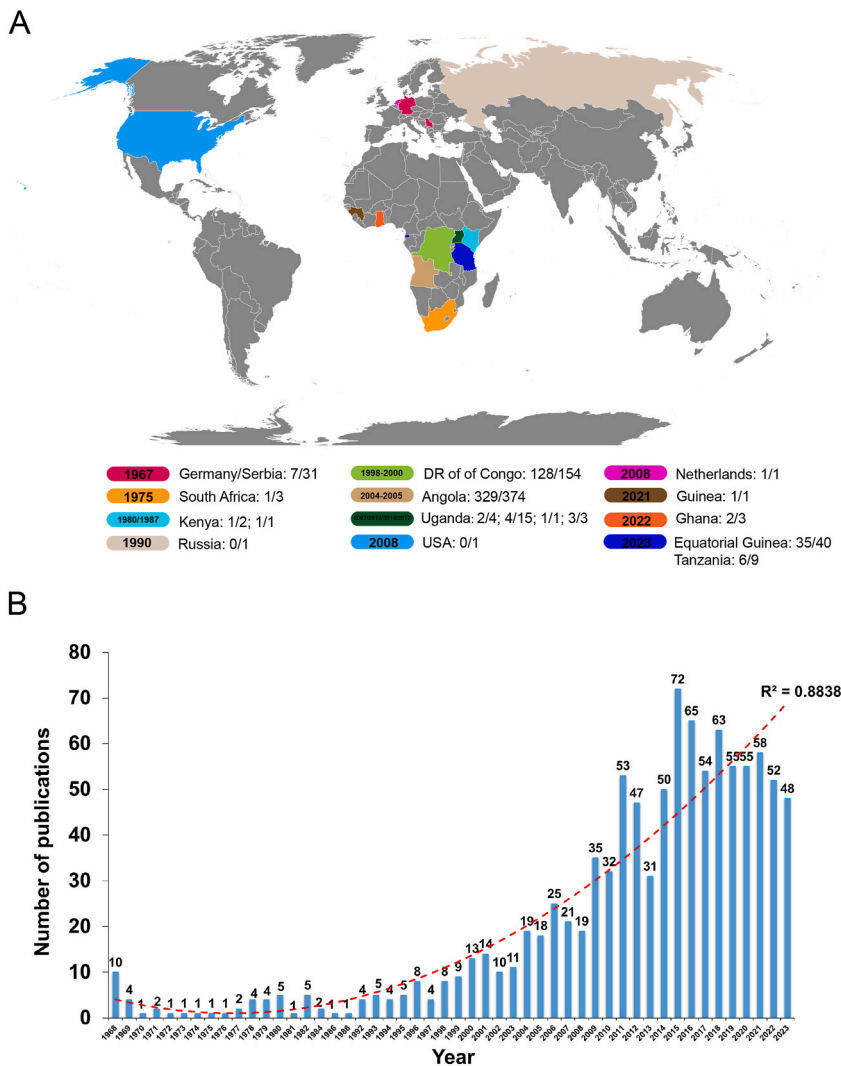


Fig. 2. (A) Map delineating the geographical dispersion of MARV across diverse epidemic occurrences. Different countries give different colors based on the corresponding confirmed cases and fatalities (B) Annual publication volume of MARV related articles from 1968 to 2023. R^2 represents the coefficient of determination for the fitting curve. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

1.6.20) [35] were harnessed to explore diverse facets of the research data.

VOSviewer a freely available tool, was employed to craft and visualize bibliometric networks and maps derived from data encompassing journal relationships, author/countries/institution collaborations, and citation patterns [35]. This process enabled the identification of research focal points by extracting keywords from bibliometric co-occurrence analysis. Parameter settings of VOSviewer were as follows: type of analysis (select one at a time), thresholds of items (based on particular situations), VOSviewer thesaurus file (merge different variants of counties/regions or keywords). VOSviewer is capable of generating three distinct visual map types: network, density, or overlay maps. These knowledge maps embody nodes representing diverse facets such as countries, institutes, or authors [36]. The interconnections among these nodes illustrate the relationships within these elements. The linkages between nodes signify associations, with several determinants influencing the node’s magnitude, including publication count, citation frequency, or occurrences. For improved differentiation, nodes and linkages are color-coded according to different clusters or their respective average appearance year (AAY) [37].

Additionally, we utilized another bibliometric software, Citespace, designed by Professor Chaomei Chen of Drexel University, for further comprehensive bibliometric analysis such as dual-map overlay of journals, cluster detection, and identification of citation bursts for references [34]. We conducted time-slicing with one or two years per slice, establishing node types (such as institution, cited reference, keyword), and pruning methods (applying pathfinder for pruning sliced networks). The default settings were maintained for other software components. CiteSpace provides a range of significant metrics, encompassing temporal measures like citation burstness, structural measures such as betweenness centrality (BC). Burstness denotes the rate of change. It tracks the frequency of an entity over time, identifying specific periods when there is a sudden shift in frequency, thus pinpointing emerging terms [38]. BC gauges how often a node (e.g., an article or author) occurs on the shortest path between other nodes, using Freeman’s BC metric. Nodes with substantial BC typically bridge different clusters and are pivotal hubs. And in the map, nodes are denoted by purple circles when their BC equals or exceeds 0.1 [39]. Additionally, in CiteSpace, clusters were generated using the “Clustering” function, systematically grouping shared co-citation pathways into clusters that represent sub-themes and specialized areas within the research field. The modularity (Q score) of a network gauges its capacity for segmentation into modules or clusters, while the silhouette (S score) validates and interprets consistency within the data clusters. Silhouette coefficients exceeding 0.3, 0.5, or 0.7 denote homogeneous, reasonable, or highly credible networks, respectively. However, a silhouette score of 1 might imply relative isolation within the corresponding cluster. Q

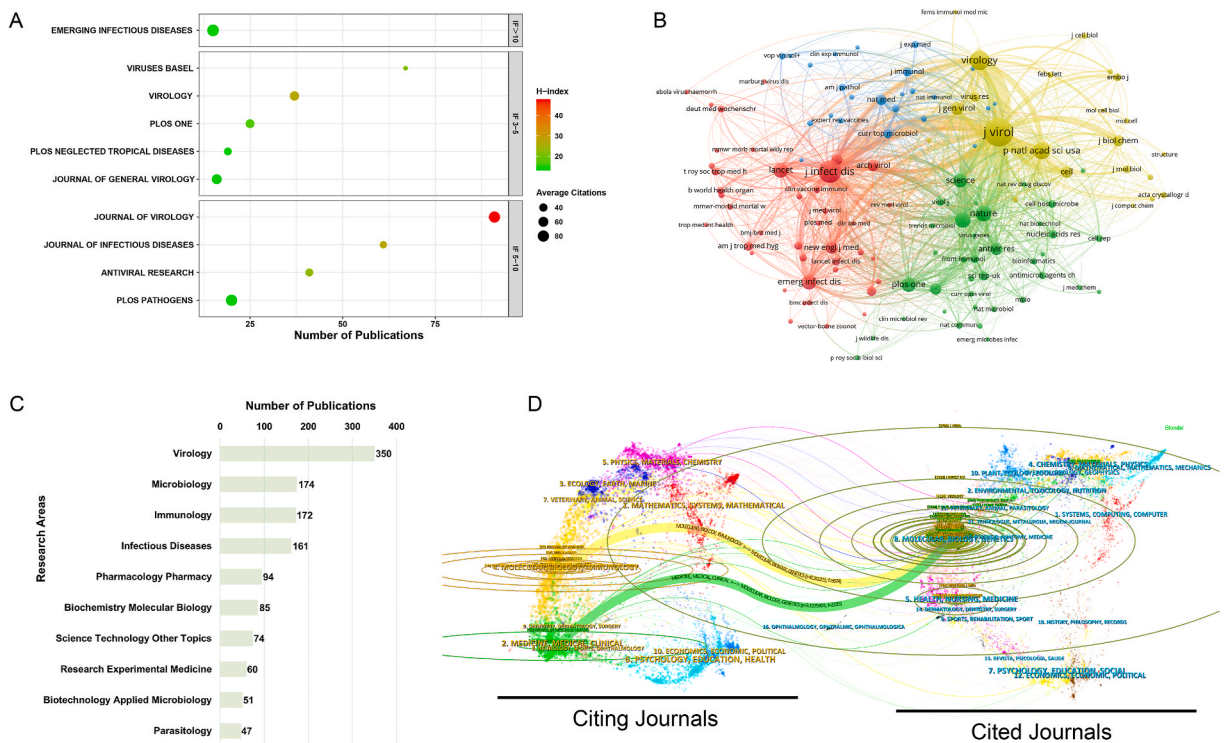


Fig. 3. (A) Top 10 most prolific journals in this field. Node size was proportional with the number of average citations and node color is relative to H-index. (B) Co-citation network among journals generated by VOSviewer. Every node symbolizes a distinct journal, with its size proportionally reflecting the volume of citations. Different colors of nodes represent different clusters. (C) The top 10 research domains ranked by their individual publication counts. (D) Dual-map overlay of journals pertinent to MARV research. The labels represented different research subjects covered by the relevant journals. The spline curves originate from the citing journals positioned on the left and extend towards the cited journals situated on the right. The width of the lines correlates with a z-score-scaled citation frequency, signifying the strength of connection between scientific domains within the analysis. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

metric spans from 0 to +1, and S metric ranges from -1 to +1. A score nearing +1 signifies optimal clustering. A Q value surpassing 0.3 indicates significant cluster structure, suggesting a well-organized network [40]. Cluster labels are derived from noun phrases in keyword lists of cited articles within each cluster via the likelihood ratio test.

3. Results

3.1. The comprehensive overview and publication trends

For a comprehensive comprehension of the global prevalence of the MARV, we summarized, in Fig. 2A, the regions affected by MARV outbreaks to date, alongside the corresponding confirmed cases and fatalities. It can be seen that MARV is mainly prevalent in Africa. According to our statistics, approximately 643 confirmed cases have been described in the literature to date, and mortality observed was 81.2% in overall patients. After screening by the above procedure, a total of 1014 papers comprising 869 original articles and 145 reviews, were encompassed. These publications collectively garnered 44673 citations as of the search date, boasting an average citations per article (ACI) of 44.06 and an H-index of 102. Visual representation in Fig. 2B delineates the annual publication volume of pertinent articles from 1968 to 2023. The fitted curves aptly illustrated an increasing growth pattern in annual publications during the 1968 to 2023 period ($R^2 = 0.8838$). For comparison, we conducted an exhaustive search for all relevant studies on another member of the Filoviridae family of Ebola virus within WoSCC (Supplementary Fig. 1). The results manifestly indicate a significantly higher quantity of publications related to the Ebola virus compared to those associated with the MARV (8042 vs 1014).

3.2. Analysis of active journals and research domains

The top 10 most prolific journals in this field were summarized in Fig. 3A. All these journals have published 392 studies, accounting for 38.7% of all 1014 publications. Of them, *Journal of Virology* published the most papers ($n = 91$), *Viruses Basel* ranked the second, with 67 papers, followed by *Journal of Infectious Diseases* ($n = 61$), and *Antiviral Research* ($n = 41$). Regarding IF, *Emerging Infectious Diseases* boasts the highest with 11.8, succeeded by *Antiviral Research* (7.6) and *Plos Pathogens* (6.7). Based on the 2023 JCR categories, half of journals are classified within Q1. In addition, when assessing a journal's impact, citation frequency often outweighs publication quantity as a superior metric. Consequently, by employing VOSviewer, we conducted a meticulous analysis of the co-citation network among journals, yielding a visual map delineating the interlinked journals in Fig. 3B. Only journals with a minimum of 50 citations

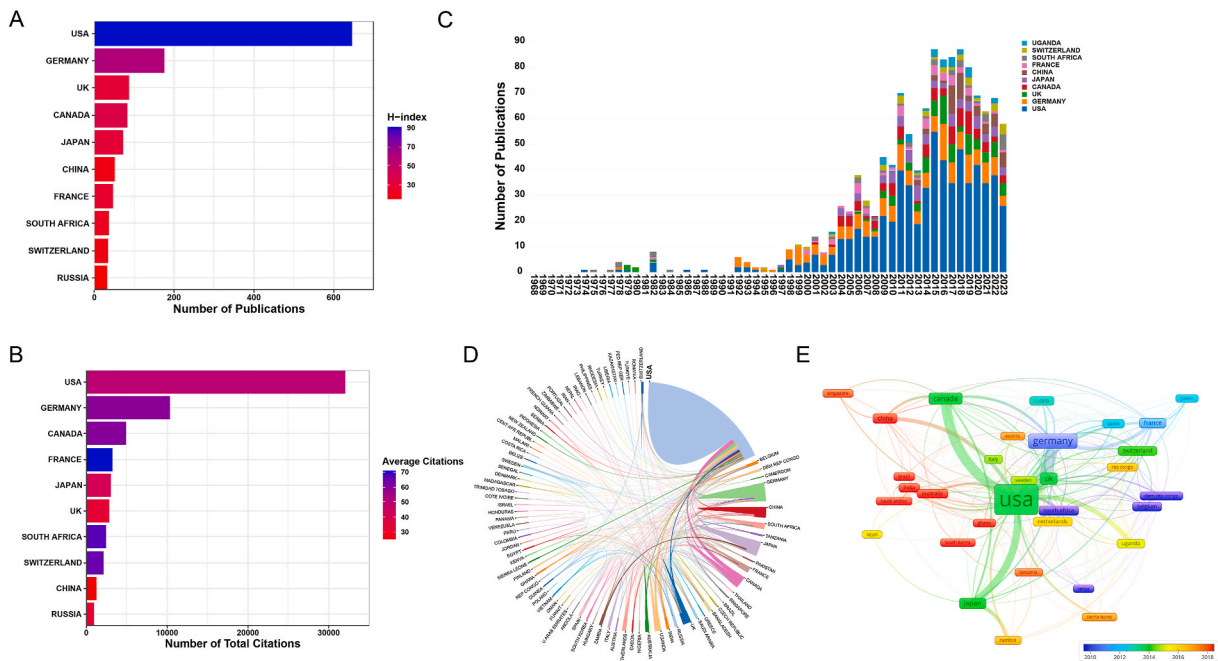


Fig. 4. (A) The top 10 countries/regions exhibiting the highest publication output within this domain. Node color is relative to H-index. (B) The cumulative and mean citation counts across these top 10 countries/regions. Node color is relative to average citations. (C) The annual publications of the foremost 10 countries/regions spanning from 1968 to 2023. (D) The international collaboration among pertinent countries/regions. The thicker the connection is, the closer the cooperation is. (E) The visualization map of country co-authorship overlays by using VOSviewer. Each node symbolizes a country/region, with its diameter proportional to the total number of publications. The color gradient signifies the average appearance year (AAV), while the line thickness denotes the strength of co-authorship connections. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

were visually represented, resulting in a network map featuring 124 nodes. The top three journals ranked by the largest TLS were listed as follows: *Journal of Virology* (TLS = 4496.37), *Journal of Infectious Diseases* (TLS = 2719.16), and *Virology* (TLS = 1958.89).

Each entry cataloged within the WoSCC receives allocation to one or multiple research areas based on journals. Examination of these research areas furnishes scholars with an instinctive grasp of the primary subjects within a given research domain. Within this dataset, a total of 60 distinct research areas were identified. Among these, the most prominently represented research areas by publication quantity were (Fig. 3C): virology (350 publications), microbiology (174 publications), immunology (172 publications), and infectious diseases (161 publications). Furthermore, as depicted in Fig. 3D, we constructed a dual-map overlay of journals pertinent to MARV research. The base map was crafted upon a compilation of 10000 journals, while the citing trajectories were subsequently derived from the input data. Collectively, the present map delineated two prominent citation trajectories. The journal citation matrices predominantly spanned two spheres: (1) medicine, medical, and clinical; (2) molecular, biology, and immunology. Notably, the most frequently cited publications emanated from journals within the realms of molecular, biology, and genetics.

3.3. Main contributors of global publications related to MARV

3.3.1. Contributions of countries/regions

Within this pool of 1014 publications, scholars from 91 diverse countries/regions have made contributions to this field, encompassing both developing and developed economies. Notably, the United States leads in the publication of research articles related to MARV research, totaling 645, followed by Germany with 175 and UK with 87. As for the H-index, the United States maintained its leading position with 91, followed by Germany and Canada, both boasting H-indices surpassing 35 (Fig. 4A). Furthermore, it is noteworthy that despite lower publication counts in certain nations, a substantial ACI were observed in Fig. 4B. Fig. 4C illustrated the yearly publications of the foremost 10 countries/regions spanning from 1968 to 2023. Evidently, the United States and Germany consistently emerged as the most prolific contributor throughout the entire study duration. Fig. 4D illustrated the international collaboration among pertinent countries/regions. Notably, researchers from the United States exhibited particularly close collaboration with counterparts from Canada, Germany, and Uganda. Fig. 4E depicted the visualization map of country co-authorship overlays by using VOSviewer. Only countries/regions contributing more than 5 papers were represented. Among the 34 countries/regions meeting this criterion, the top three, namely the United States, Germany, and UK exhibited the highest TLS, affirming their dominant positions in this field. Moreover, the node color in this visualization denotes the average appearance year (AAV) for each country, showcased in the color gradient at the lower right corner. Notably, countries were depicted in dark blue, indicating their early



Fig. 5. (A) Top 10 institutions and their corresponding publication counts. (B) Network visualization map of institutional collaboration analysis generated using CiteSpace. (C) Top 10 institutions with the highest betweenness centrality (BC) values. Nodes with a BC value ≥ 0.1 are marked in red color. (D) The distribution of the foremost 8 funding sources. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

engagement in MARV research. Conversely, nodes with red color suggest their relatively recent involvement in this field.

3.3.2. Contributions of institutions and funding agencies

In the analysis of institutions, more than 1300 establishments have contributed to the published research within this field. Fig. 5A showcased the top 10 institutions and their corresponding publication counts. Notably, among these leading institutions, seven institutions from the United States, two from Canada, along with one each from Germany. National Institutes of Health (NIH) emerged as the foremost contributor in terms of publication count, followed closely by NIH National Institute of Allergy & Infectious Diseases (NIAID), and University of Texas System. The network visualization map depicting institutional collaboration was generated using CiteSpace (Fig. 5B). Centers for Disease Control & Prevention exhibited the highest centrality, with a BC value of 0.37, followed by Philipps University Marburg (0.36), and NIAID (0.18) (Fig. 5C). Fig. 5D illustrated the distribution of the foremost 8 funding sources. Among them, five of these are from the United States.

3.3.3. Contributions of authors

Subsequent to an initial analysis, it was discerned that over 4500 authors actively contributed to the 1014 studies. To refine the co-authorship cluster visualization in Fig. 6A, focus was directed towards authors contributing to over 10 publications. Authors sharing analogous color-coding in the diagram exhibit analogous co-authorship traits, thus forming 7 distinct research clusters. These clusters were centered around a select group of highly prolific authors, fostering extensive publications. Within this cohort, the top 10 individuals displaying noteworthy productivity in article publications could potentially serve as valuable research collaborators in the field. Depicted in Fig. 6B, Feldmann Heinz, an internationally recognized virologist and chief of the Laboratory of Virology at Rocky Mountain Laboratories, emerges as the most prolific author, closely followed by Bavari Sina from United States Army Medical Research Institute of Infectious Diseases and Geisbert Thomas W from the University of Texas Medical Branch at Galveston. Remarkably, eight-tenths of the top 10 authors originated from the United States, while the other two were from Germany. Regarding ACI, Nichol Stuart T from Centers for Disease Control & Prevention secured the top rank with 95.85. Furthermore, Fig. 6C visually represented the network

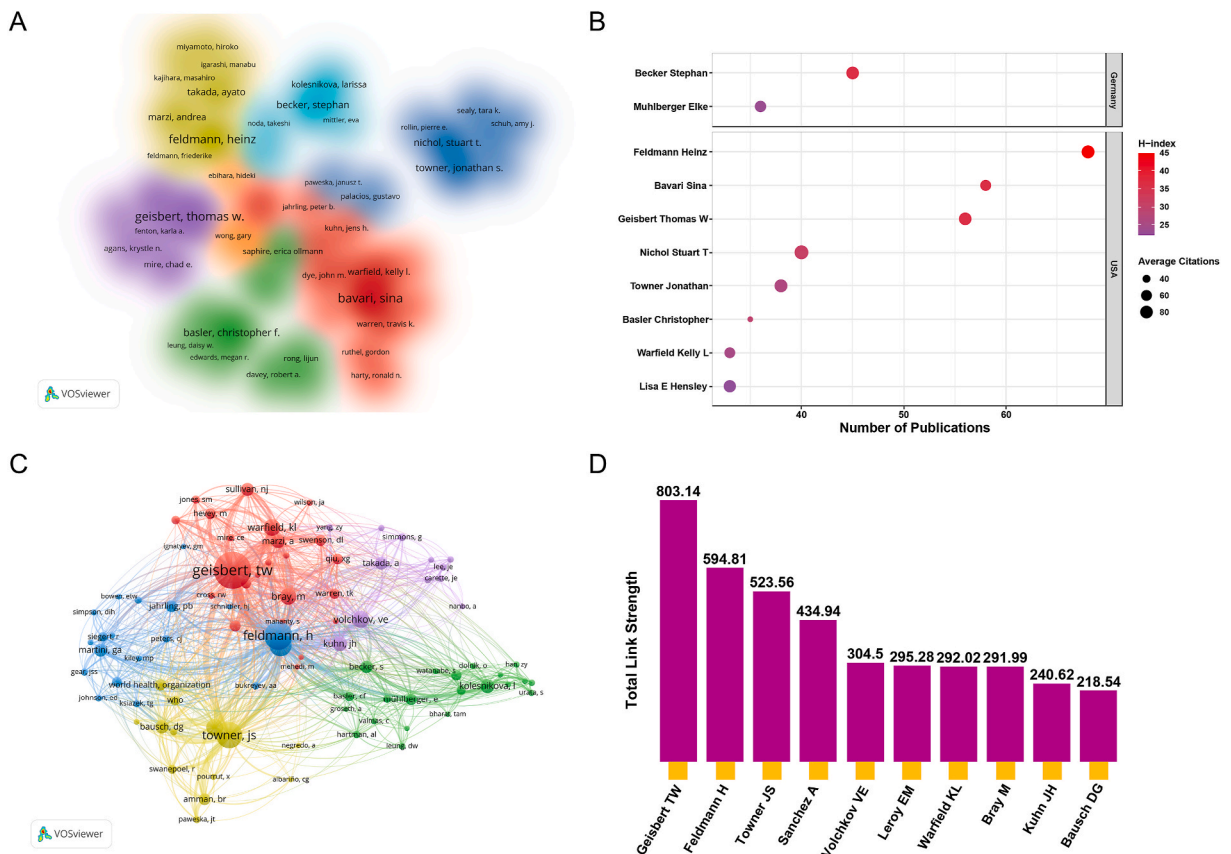


Fig. 6. (A) Co-authorship cluster visualization map produced by VOSviewer. Authors indicated by different colors shows the cooperation cluster between different authors. (B) Dot plot showcasing the top 10 authors by publication count. Node size is proportional with the number of average citations and node color is relative to H-index (C) Network visualization map depicting co-cited authors. Every node symbolizes a distinct author, with its size proportionally reflecting the volume of citations. Different colors of nodes represent different clusters. (D) Leading 10 authors identified based on Total Link Strength (TLS). (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

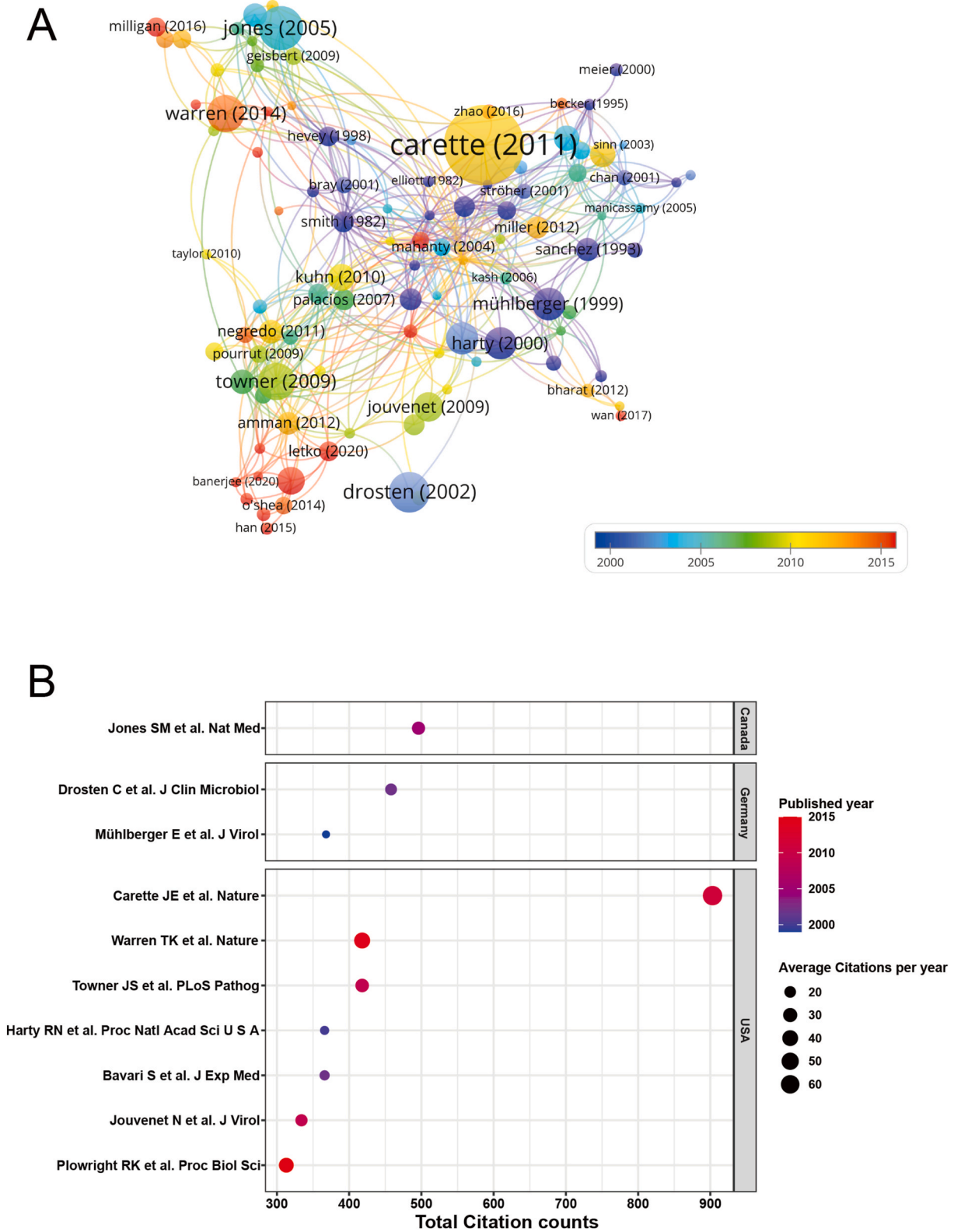


Fig. 7. (A) Network visualization map delineating paper citation analysis. (B) Characteristics of the top 10 extensively cited studies in the realm of MARV research.

map of co-cited author relationships, where each node correlates to a cited author and is proportionate to the citations received. Fig. 6D succinctly outlines the top 10 authors based on TLS, with Geisbert TW, Feldmann H, and Towner JS attaining the highest ranks.

3.4. Analysis of highly cited literature

Highly cited papers often signify significant influence and importance within a particular field or academic realm. They may encompass pioneering ideas, methodological innovations, or critical solutions to problems, thus guiding future academic explorations. Fig. 7A presented a network visualization map delineating paper citation analysis. Enlarged nodes symbolize heightened citation counts, indicating the influence of papers within the citation network. This visual representation offers a lucid portrayal of the relative citation frequencies for each study, enabling researchers to identify studies garnering substantial citation counts. In Fig. 7B, the top 10 extensively cited papers in this domain were showcased. These significantly referenced papers span from 1999 to 2015. Notably, seven-tenths of the first authors in these top 10 studies originate from the United States. Among these, the most prominently cited publication authored by Carette et al., in 2011, amassed an impressive 903 citations. Following closely, the study by Jones et al. secured the second position with 496 citations, while the paper by Drosten et al. claimed the third spot with 458 citations.

3.5. Co-cited references and reference burst

The co-citation relationship indicates the simultaneous presence of two articles within the reference list of a paper. Reference co-citation analysis is frequently utilized to delineate the predominant research themes within a specific field. In Fig. 8A, a graphical representation of the co-citation network analysis of references is depicted. The Modularity Q, quantified at 0.7515, along with a mean Silhouette S of 0.916, signify an impressive clustering effect and substantial network uniformity as revealed by the analytical outcomes. Furthermore, Fig. 8B showed the timeline view of co-citation references, capturing the evolving research focal points. Ten distinct clusters emerged from the clustering outcomes. Along the line, nodes represent cited references, while the purple-labeled ones signify earlier appearing clusters, contrasting with the red-labeled clusters indicating current research focuses. From the resulting plots in Fig. 8B, “single-shot chad3-marv vaccine (#4)” and “small molecule drug development (#6)” have become the latest research hotspots. Fig. 8C distinctly illustrated the top 30 references displaying the most robust citation bursts. Here, the blue line delineates the time interval, while the red segment highlights the duration characterized by the burst of references.

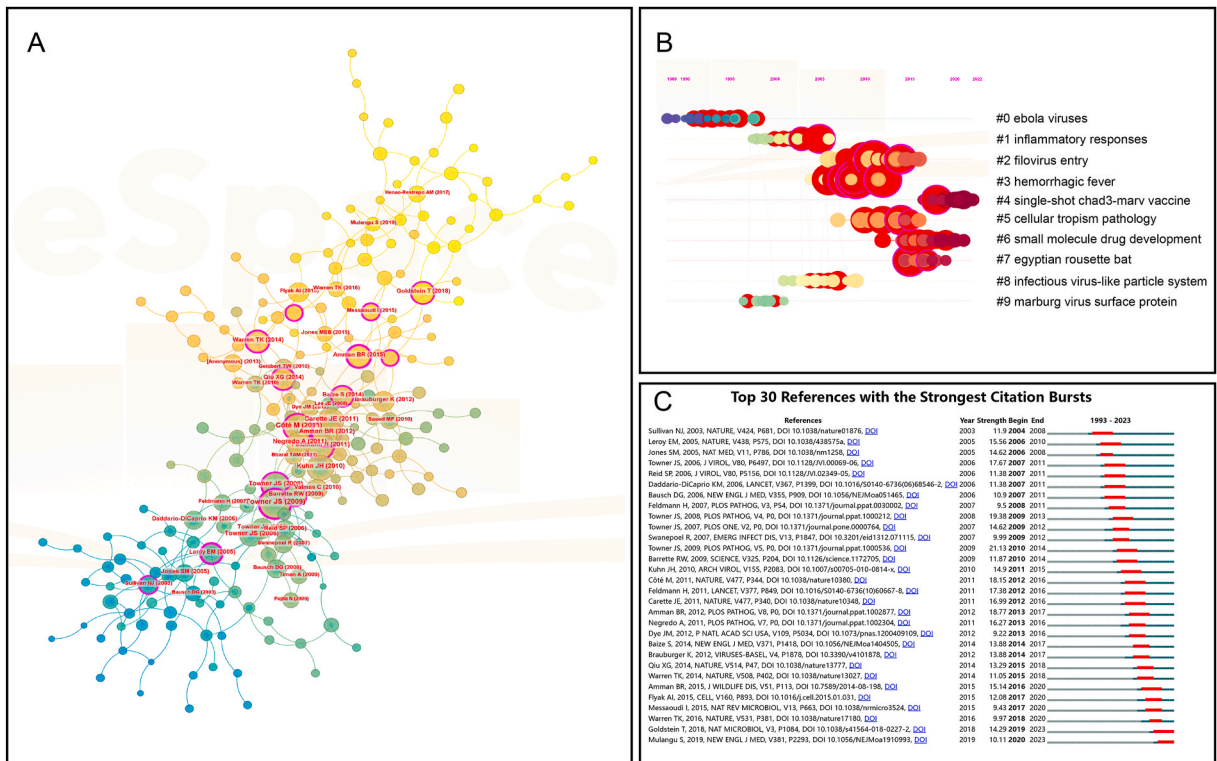


Fig. 8. (A) Network visualization map of references co-citation analysis. (B) The timeline view of references co-citation analysis. It delineates ten distinct clusters, each labeled and color-coded on the right side. Along the line, nodes represent cited references, while the purple-labeled ones signify earlier appearing clusters, contrasting with the red-labeled clusters indicating current research focuses. (C) Top 30 references exhibiting the strongest citation bursts. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

3.6. Keywords co-occurrence and keywords burst

Through using VOSviewer software, a keyword co-occurrence map was developed. Following the amalgamation of synonymous keywords and the manual exclusion of general or ubiquitous terms, a total of 161 nodes with a minimum of 10 co-occurrences were visualized in a density visualization map in Fig. 9A. Among them, we have summarized the top 20 highest-frequency keywords in Fig. 9B. The most frequently used keywords were Marburg virus, Ebola virus, filovirus, hemorrhagic-fever, infection, glycoproteins, nonhuman-primates, pathogenesis, and so on. Furthermore, within VOSviewer, the clustering feature enables the segmentation of the comprehensive co-occurrence network into distinct clusters. Keywords exhibiting stronger correlations tend to cluster together, denoted by identical colors. Illustrated in the network visualization map (Fig. 10A), the selected keywords were categorized into four

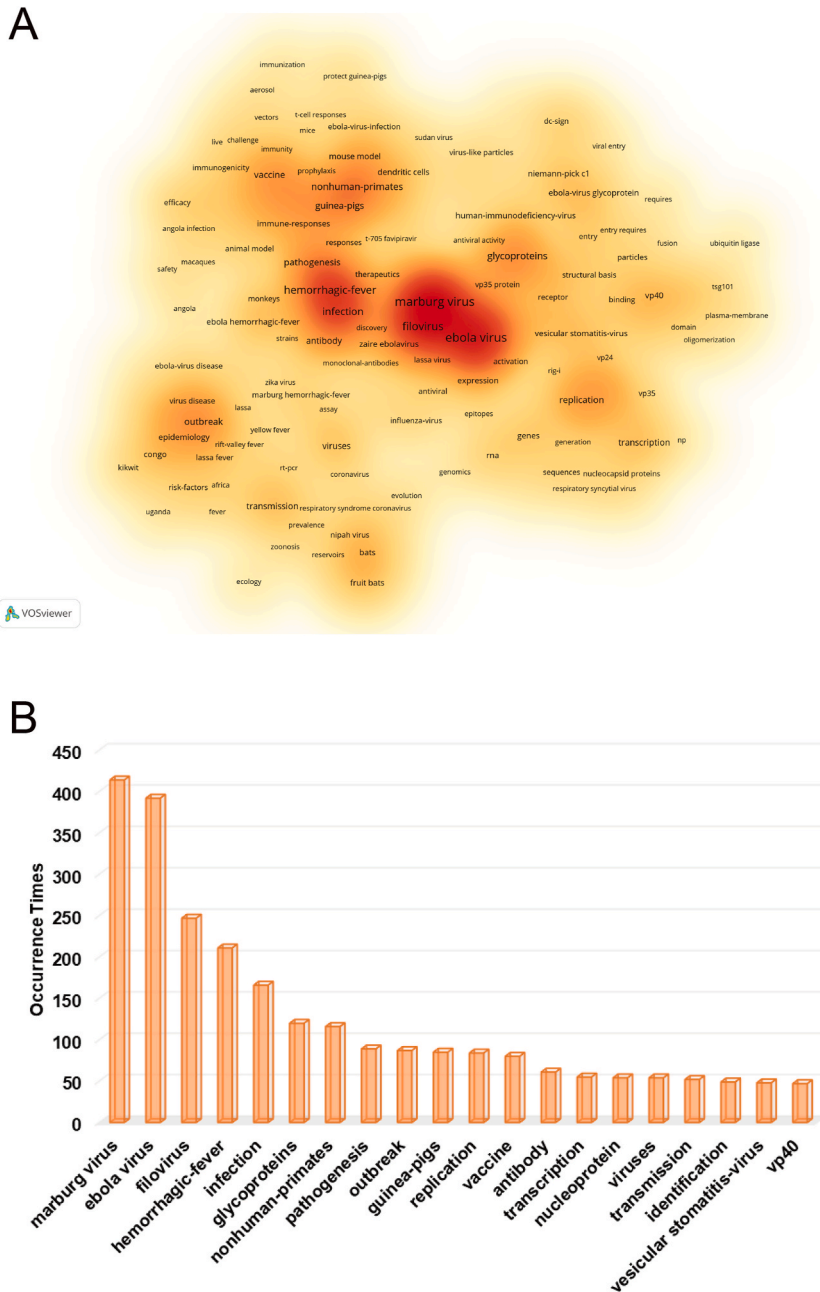


Fig. 9. (A) The density visualization map delineates keyword co-occurrence analysis. Deeper red hues correspond to vibrant research domains, showcasing higher keyword co-occurrence frequencies, while lighter yellow hues signify less active areas with lower keyword co-occurrence frequencies. (B) Top 20 keywords with the highest frequencies. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

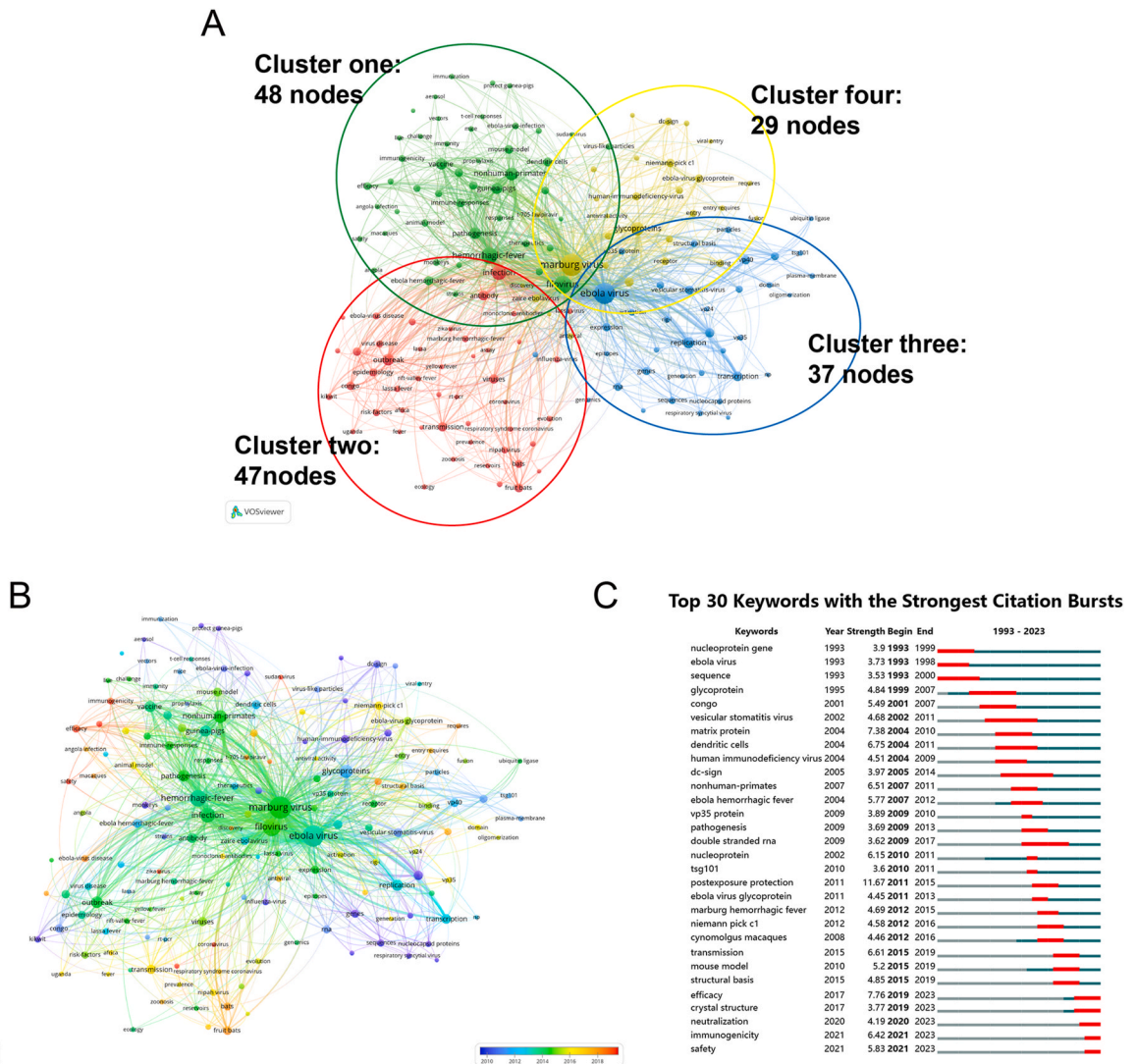


Fig. 10. (A) Visualization of co-occurrence analysis pertaining to MARV research. Each keyword is annotated with the node size indicating its frequency of occurrence. Nodes of larger size represent higher co-occurrence frequency of specific keywords. VOS viewer employs distinct colors to demarcate keywords, with node and label colors signifying their respective clusters. Keywords sharing a color belong to the same cluster, thereby grouping closely associated terms. Proximity in the network reflects the frequency of co-occurrence between keywords, with higher occurrences positioning them closer within the network. (B) Overlay visualization map of keyword distribution. The blue hue indicates earlier appearances, while the yellow points denote later occurrences. The node and label meanings in this representation align with those in Fig. 10A. Yet, the node color in this rendition denotes the AAY of the keyword within the article, as indicated by the color gradient provided in the lower right corner. (C) Top 30 keywords exhibiting the strongest citation bursts. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

primary themes: cluster 1 (green nodes, positioned on the upper left of the network), cluster 2 (red nodes, located on the bottom left of the network), cluster 3 (blue nodes, situated on the bottom right of the network), and cluster 4 (yellow nodes, positioned on the upper right of the network). Fig. 10B presented an overlay visualization map depicting the evolution of keywords over time. Highlighted by red nodes, these indicate emerging keywords that might signify current and potential research focal points. The following keywords marked with red color such as “double blind”, “efficacy”, “safety”, “immunogenicity”, “inhibitors”, “Egyptian rousette bat”, etc., seemed to represent the current research frontiers. In addition, CiteSpace was also used to identify emerging keywords, and Fig. 10C showcased the top 30 keywords exhibiting the strongest citation bursts. Of note, the bursts of following topics including “efficacy (2019–2023)”, “crystal structure (2019–2023)”, “neutralization (2020–2023)”, “immunogenicity (2021–2023)”, “safety (2021–2023)”, are still ongoing, which hold significant potential to remain at the forefront of research focus in the future.

4. Discussion

The utilization of bibliometric analysis in the field of infectious diseases has emerged as a pivotal tool for comprehensively understanding and assessing research dynamics [20]. By scrutinizing literature citations, publication trends, and the evolutionary trajectory of research themes, it illuminates pivotal research trajectories and developmental patterns pertinent to specific infectious diseases [17,18]. Especially during the global pandemic of COVID-19, the number of relevant studies has increased rapidly. Many scholars have utilized the bibliometric method to aid in comprehending the prevalence of COVID-19 and the evolution of treatment and prevention approaches, especially vaccines [21–26]. Moreover, the application of bibliometric analysis could also facilitate an evaluation of scientific influence and research quality within specific domains and direct scientists and policymakers in establishing priority research areas while providing decision-making support for infectious disease prevention and control strategies [18–20]. However, to our knowledge, an exhaustive analysis of the literature related to MARV is still lacking. In this study, WoSCC database was selected as the primary data source and subsequently employed multiple bibliometric software to visually represent the bibliometric networks encompassing literature pertinent to MARV research spanning the period between 1968 and 2023.

For a comprehensive understanding of the global prevalence of the MARV, this study synthesized the regions impacted by MARV outbreaks to date, along with the corresponding confirmed cases and fatalities. This visual representation in Fig. 2A distinctly highlights the predominant prevalence of MARV within the African regions. Our statistical analysis has documented approximately 643 confirmed cases in the literature to date, portraying an overall mortality rate of 81.2 % among affected patients. Our data directly underscore the significant impact of MARV, particularly evident within the African territories. As for the potential reasons, the MARV is commonly found in non-human primates, serving as the natural reservoir for this pathogen [41]. Human infection is facilitated through contact with these animals or handling their bodily fluids and tissues. Certain traditional lifestyles and cultural habits in specific regions of Africa may heighten the chances of exposure to potential hosts, thereby escalating the risk of infection. Moreover, inadequate medical facilities, protective equipment, and sanitation measures could facilitate the virus's spread within communities. Deficiencies in healthcare and infrastructure in certain African regions may contribute to the rapid dissemination of outbreaks. The current scenario suggests the potential pandemic emergence of MARV, evidenced by its spread from Equatorial Guinea to Tanzania [12]. As an RNA virus, the MARV is susceptible to mutations akin to COVID-19. These mutations might augment the MARV's potency in terms of virulence, transmissibility, mortality, and morbidity rates [42]. Over the last few years, all of us have witnessed the catastrophic repercussions stemming from the mutations of the COVID-19, wherein these variations have amplified the virus's transmissibility, posing a grave threat to global public health [43]. This urgency compels a heightened focus on diseases akin to the MARV, recognizing that viral mutations could significantly alter their characteristics and modes of transmission, posing unpredictable risks to human health [44,45]. However, based on our results, despite the noticeable surge in MARV-related research in recent years, a significant disparity persists when comparing the quantity of studies to those related to Ebola (8042 vs 1014). A previous bibliometric study performed by Cruz-Calderón et al. [46] summarized the global research trend about Ebola. A total of 7262 Ebola-associated items were retrieved in their search. This discrepancy unequivocally highlights the insufficient attention devoted to MARV-related research in the past few years. Hence, our findings strongly advocate for intensified research endeavors on MARV to proactively address this impending public health menace.

The analysis of academic journal distribution serves as a window into the key publications within a particular domain, guiding scholars in the selection of the most suitable academic outlets for disseminating their research findings [47]. Therefore, the top 10 most prolific journals have been summarized in this field. Indicators like IF, JCR category, and citations serve as effective benchmarks for evaluating journal quality. Unsurprisingly, most of the leading 10 journals were grouped in the virus category. Of them, *Journal of Virology* published the most papers. Besides that, journal co-citation analysis has identified the most influential journals with the most citations in the MARV domain. Co-citation analysis establishes associations between items according to their co-cited frequency, while TLS serves as a metric to evaluate the overall connection intensity between them. The top three journals ranked by the largest TLS were *Journal of Virology*, *Journal of Infectious Diseases*, and *Virology*. The outcomes unveiled a noteworthy trend: research delineating MARV, when published in these journals, stands poised for higher citation rates and substantial recognition. Notably, *Journal of Virology* holds the foremost position, boasting the most substantial TLS among co-cited journals. This achievement might be attributed to two highly cited studies in this field [48,49]. Among them, Mühlberger et al. [49] has compared the transcription and replication strategies of MARV and Ebola virus. This comparison between MARV and Ebola virus emphasized similarities in morphology, genome structure, and protein composition. Yet, distinct dependencies in nucleocapsid proteins for replication and transcription were revealed, with VP30 being essential specifically for Ebola virus transcription, distinguishing it from MARV. While the other study by Jouvenet et al. [48] found that tetherin, a type I interferon-induced antiretroviral protein, could inhibit the release of particles assembled using filovirus matrix proteins from MARV and Ebola virus. In addition, it is not hard to see that within the most prolific and impactful journals, most of them hailed from Western European and North American nations, signifying the predominant influence of publications from Euro-American regions in this domain.

When it comes to the main contributors in this field, there is no doubt that the United States has occupied the dominant position. Prior investigations proposed that disparities in publication quantities across nations may predominantly stem from economic factors rather than population size [50]. This assertion was reaffirmed by the national allocation of the top 8 funding agencies in this domain, with five originating from the United States. These funding sources have played a pivotal role in facilitating research efforts, propelling advancements in the field of MARV. As matter of fact, before the Ebola epidemic from 2013 to 2016, despite the catastrophic impact of filovirus infections on public health, there was a limited allocation of funds from the public sector towards developing therapeutic drugs [51,52]. Consequently, research on vaccines and treatment methods for filoviruses during this period remained relatively scarce. However, since 2016, there has been a substantial increase in funding for both foundational and translational research on filoviruses,

owing to biodefense initiatives and research grants [53]. This shift signifies a strengthened focus on studying filoviruses and similar pathogens, propelling advancements in vaccines and treatments targeting these threats. The surge in funding has provided the scientific community with greater opportunities to expedite the understanding of viral pathobiology and seek effective interventions.

Apart from financial and policy-related assistance, top-tier research institutions and distinguished scientists significantly propel the progress and evolution of a particular field. In the landscape of institutions engaged in MARV research, top positions were held by U.S.-based establishments such as the NIH, NIAID, and University of Texas System based on publication frequency. Meanwhile, amidst the top 10 extensively referenced studies in the MARV research domain, seven of these studies prominently featured a first author affiliated with scientific research institutions based in the United States. Regarding prolific authors, 80 % of the top 10 most productive authors hailed from the United States. Notably, in this study period, Feldmann Heinz [54,55], an internationally recognized virologist and chief of the Laboratory of Virology at Rocky Mountain Laboratories, emerges as the most prolific author, closely followed by Bavari Sina [56,57] from United States Army Medical Research Institute of Infectious Diseases and Geisbert Thomas W [58] from the University of Texas Medical Branch at Galveston. Moreover, author co-citation analysis, a prevalent method, was employed to unveil prominent figures within the co-citation network of this field [20]. Authors frequently cited are deemed to wield substantial influence and impact. Our identification of highly influential authors, those garnering at least 70 citations, revealed that the top three, including Geisbert TW, Feldmann H, and Towner JS. Hence, these insights underscore the United States' enduring prominence in both the quantity and quality of publications in this sphere, partly attributed to the contributions of these influential institutions and authors.

However, it is still noteworthy that the map in Fig. 5B illustrated discernible levels of collaboration and interaction among diverse research institutions globally. Particularly close cooperation is evident between institutions in Europe and America, while collaborations among other institutions appear more geographically restricted, often confined within individual countries or specific regions. In grappling with the challenges posed by infectious diseases, the irrefutable significance of global collaboration has been exemplified vividly through the case of COVID-19 [59]. This pandemic swiftly disseminated worldwide within a concise timeframe, underscoring the immediacy and indispensability of international cooperation. Nations have joined forces in endeavors encompassing viral diagnostics, medical equipment production, scientific research, and vaccine development, collectively confronting this public health exigency [60]. For instance, scientists transcended borders, sharing viral genomic sequence data to aid in devising more efficacious detection methodologies and vaccines. Furthermore, governments, health institutions, and international organizations have fortified information exchange and resource allocation, offering targeted support to affected regions [59,60].

Quantifying the relative impact of scientific papers in a subject area, citation counts serve as a common evaluative metric in bibliometric analysis. The number of citations a paper receives typically correlates with its influence and recognition [61,62]. Highly cited publications are often presumed to represent high-quality studies characterized by significant influence and innovation within a specific field [19–21]. These papers are considered foundational and pivotal readings for scholars aiming to delve into the domain. Fig. 7B delineates the specifics of the top 10 highly cited articles within the research area of MARV [48,49,63–70]. After scrutinizing the principal topics addressed in all these highly cited studies, these research directions including the identification of MARV natural reservoir and exploration of virus spillover mechanisms, the mechanisms behind viral transcription, replication, and budding, live attenuated recombinant vaccine, rapid detection and quantification technology, broad-spectrum antiviral drugs such as BCX4430 [66] and Tetherin [48], have garnered more attention. In addition, although the top 10 highly cited articles mentioned above have served as pivotal contributions due to their significance, a broad trend suggests obvious correlation between the duration since publication and the citation count. This implies that articles published earlier may tend to accumulate more citations. Consequently, relying solely on citation counts may overlook recent high-quality studies. To monitor the evolution of research focal points, document burst analysis was conducted using CiteSpace. Typically, articles with citation bursts signify heightened attention from related academic spheres during a specific timeframe. As shown in Fig. 8C, references with citation bursts first appeared in 2004 due to the study published in 2003, and continued through 5 years [71]. In addition, the reference exhibited the highest burst strength starting from 2010, and was study published by Towner et al., in 2009 [67]. And this is also one of the highly cited studies. The study garnered considerable attention for its pioneering identification of the Egyptian fruit bats as a potential primary natural reservoir and source of the MARV. Apart from the burst function of references, by using the log-likelihood ratio (LLR) test algorithm, CiteSpace could conduct automatic clustering and merging of references extracted from the titles of these articles. Fig. 8B showed the timeline view of co-citation references, capturing the evolving research focal points. Ten distinct clusters emerged from the clustering outcomes. Evaluating the mean years within these clusters reveals a shift in research focus towards “single-shot chad3-marv vaccine (#4)” and “small molecule drug development (#6)”. These results again illustrated that the development of reliable and robust vaccine and treatment strategies were the top priorities of current studies.

Take vaccine research as an example, at the initial discovery of the MARV, technological limitations led to the primary development of vaccines in an inactivated form. However, animal experimentation revealed its limited protective efficacy, conferring approximately 40 % protection to guinea pigs and 50 % to non-human primates against homologous viral assaults [72]. Consequently, acknowledging the drawbacks of low efficacy, short duration of protection, and heightened risks associated with inactivated vaccines, researchers pivoted their focus toward the development of alternative vaccines such as adenovirus vector vaccine, recombinant vesicular stomatitis virus-based vaccine, DNA vaccine, and so on [73–76]. Among them, the Ad26.ZEBOV/MV vaccine, utilizing an adenovirus as a vector, presents antigens targeting the Ebola and MARV [72]. Following encouraging outcomes in preclinical trials, the vaccine is presently undergoing clinical evaluation. While the chimpanzee adenovirus type 3-vectored Marburg virus (cAd3-Marburg) vaccine is presently one of the vaccines that has entered phase I clinical trials. The inaugural human trial of the cAd3-Marburg vaccine demonstrated its safety and immunogenicity, exhibiting a safety profile akin to previously assessed cAd3-vectored filovirus vaccines [77]. Following a single vaccination, 95 % of participants elicited a glycoprotein-specific antibody response at the 4-week mark, persisting in 70 % of participants at the 48-week assessment. The development of a MARV vaccine stands as a pivotal measure in

averting future pandemics. Despite the plethora of methodologies available for vaccine production, authorities have yet to sanction any therapeutic modalities or vaccines specifically targeting the MARV [78,79]. In 2018, the WHO designated the MARV as a priority pathogen requiring urgent development of vaccines. Furthermore, in recent years, multiple African nations have successively reported cases of human infection with the MARV, indicating a trend of epidemic spread. Hence, expediting research into MARV vaccines is of imminent necessity [80].

Moreover, keywords serve as standardized representatives chosen to encapsulate a paper's subject matter. Keyword co-occurrence analysis, a prevalent bibliometric approach, illuminates pivotal research terms that epitomize core content, offering a structured depiction of knowledge frameworks and thematic evolution within a specific domain [81]. From 1014 papers, a corpus of 161 keywords with a minimum of 10 co-occurrences was compiled. Among them, we have summarized the top 20 highest-frequency keywords in Fig. 9B. The most frequently used keywords were Marburg virus, Ebola virus, filovirus, hemorrhagic-fever, infection, glycoproteins, nonhuman-primates, pathogenesis, and so on. Within bibliometric research, the co-occurrence analysis of keywords serves to delineate primary research clusters and the thematic focus within a given domain. This investigation's findings revealed a categorization of keywords into four distinct clusters: cluster 1, encompassing the study of vaccines, emerged as the largest cluster, exploring animal models for vaccine research, vaccine safety, effectiveness, and immunogenicity etc. Cluster 2, dedicated to epidemiology of MARV, comprised 47 keywords. Primary terms included outbreak, transmission, fruit bats, epidemiology, and so on. The third cluster, comprised of 37 keywords, concentrated on the viral transmission, transcription, and replication mechanisms, featuring terms like VP40, VP35, replication, transcription, activation. Lastly, Cluster 4, regarding glycoprotein-related researches. In addition, Fig. 10B and C provided a temporal visualization of keyword occurrences based on their AAY and burst period, respectively, offering a time-based perspective within distinct zones. Combination of the both results, the following keywords such as "double blind", "efficacy", "safety", "immunogenicity", "inhibitors", "Egyptian rousette bat", "neutralization", "crystal structure", seemed to represent the current research frontiers and hold significant potential to remain at the forefront of research focus in the future. Taken together, these areas might encompass the safety and efficacy evaluation of clinical trials [79,82], development of inhibitors to curtail further viral spread [83,84], deeper understanding of vaccine immunogenicity [85], examining the role of neutralizing antibodies in the treatment of MARV [86,87], as well as virus-host association studies [88].

5. Limitations

Similar to other bibliometric investigations, this study exhibits certain limitations. Primarily, to execute bibliometric analysis, bibliographic data extraction necessitates databases such as WoSCC, Scopus, and PubMed [89]. Given the diverse formats of bibliographic data, ongoing bibliometric research typically selects a single database for analysis. For this study, WoSCC was exclusively utilized for data retrieval. In earlier sections, we have provided a comprehensive rationale for the selection of this database [29,30]. However, WoSCC may not cover all relevant articles, potentially introducing bias into the results. Secondly, the data extracted from the WoSCC database may exhibit a delay in incorporating the latest publications. In addition, due to software limitations, we could not evaluate the quality of publications and assigned equal weights to high- and low-quality publications. Despite these outlined constraints, bibliometric analysis persists as a valuable tool for garnering a comprehensive and insightful understanding of the research panorama within a particular field.

6. Conclusion

When discussing global viral infectious diseases, Ebola virus has historically garnered extensive attention, yet similarly challenging viruses like MARV have not received comparable focus. This study delves into the global landscape of MARV, marking the comprehensive analysis of its research progress and pertinent focal points to date. Our results showed that, since the early 21st century, there has been a notable surge in publications concerning MARV. However, compared to the attention garnered by the Ebola virus, MARV remains inadequately highlighted. The United States stands at the forefront of this discipline, having dedicated substantial financial, and human resources to scientific inquiry. Present research within the MARV domain revolves around several key aspects: foremost, the development of prophylactic vaccines stands as a primary endeavor in curbing viral dissemination. Secondly, the exploration of targeted antiviral therapies, especially small-molecule antivirals or MARV-specific monoclonal antibodies constitutes a vital strategy in addressing MARV infections. Furthermore, a thorough comprehension of viral transmission, transcription, and replication mechanisms stands as a focal point in current research. Looking ahead, future studies on MARV are anticipated to expand into novel arenas. These areas might encompass the safety and efficacy evaluation of clinical trials, development of inhibitors to curtail further viral spread, deeper understanding of vaccine immunogenicity, as well as examining the role of neutralizing antibodies in the treatment of MARV. All in all, this investigation delineated prevalent challenges and constraints in the field, offering potential resolutions and novel ideas as guiding references for subsequent research endeavors in this area.

Data availability statement

The authors declare that database used in the study is from publicly literature, or are available from the corresponding author on written request.

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CRediT authorship contribution statement

Yuanjun Lyu: Writing – original draft, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Wanqing Li:** Writing – original draft, Software, Resources, Methodology, Investigation, Data curation. **Qiang Guo:** Software, Resources, Data curation, Conceptualization. **Haiyang Wu:** Writing – review & editing, Validation, Software, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.heliyon.2024.e29691>.

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