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Knowledge mapping of childhood infectious mononucleosis: a bibliometric analysis for the twenty-first century

Zhengjiu Cui¹, Jinjuan Wang², Juanjuan Diao², Leiming Xi^{2*} and Yueli Pan²

Abstract

Background The incidence of infectious mononucleosis (IM) has increased in recent years, particularly in the pediatric population, and there are currently no specific drugs available, posing a threat to the lives and health of children worldwide. Although some results have been published, there is a lack of systematic review and summarization of current research.

Methods Based on screening criteria, literature on IM in children from 2000 to 2023 was retrieved from the Web of Science Core Collection. The included literature's indicators (country, institution, journal, author, keywords, and references) were analyzed and visualized using Citespace, VOSviewer software, and the Bibliometrix program package.

Results A total of 538 eligible publications were included in this study. The number of publications has been on an upward trend during this century, with great potential for future growth. The countries with the most publications are the USA and China, and Capital Medical University is the most contributing institution. Hialgrim, Henrik and Cohen, Jeffrey, I are among the field's most influential authors and co-cited authors. Among the major journals, the JOURNAL OF MEDICAL VIROLOGY had the highest output and the JOURNAL OF INFECTIOUS DISEASES. was the most frequently cited. The reference with the highest outbreak intensity was Ramagopalan, SV, LANCET NEUROLOGY, 2010. Through in-depth analysis of the keywords, we conclude that the characteristics of diagnosis and assessment of IM, the association of IM with other diseases, and interventions for IM are the current hot topics of research in the field and that the pathogenesis of IM due to EBV is a cutting-edge topic in the field. This study also analyzes the reasons for geographical research differences and proposes a new "increasing quantity-improving quality-integrating" cooperation model.

Conclusion This study's hotspots and frontiers reflect the current status and trends in pediatric IM, and these findings provide important insights to guide future research and optimize therapeutic strategies. In the future, there is a need to strengthen international collaboration and cooperation, conduct RCTs with large sample sizes, and promote the development of new drugs in mechanism research.

Keywords Infectious mononucleosis, Bibliometric analysis, Visual analytics, Trends, Cooperation, Web of science

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Introduction

Infectious mononucleosis (IM) is a lymphoproliferative disorder that most often affects adolescents and adults between the ages of 15 and 24 years. In children, it is mainly induced by infection with the Epstein-Barr virus (EBV), primarily asymptomatic in most people when first infected with it, with an incubation period of



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30-50 days [1]. EBV is a human lymphocyte-loving herpesvirus with an envelope and double-stranded DNA and is transmitted primarily through saliva, blood transfusions, and organ transplants [2]. It triggers subacute or acute proliferative changes in the monocyte-macrophage system, which manifests itself in the classic triad of irregular fever, cervical lymph node enlargement, and pharyngitis, which may be accompanied by oedema of the eyelids, hepatosplenomegaly, and malaise, and the typical peripheral blood features of increased lymphocytes and allogeneic lymphocytes [3]. Prior to the onset of puberty, primary EBV infection is usually associated with asymptomatic or mild symptoms. At present, there is no specific treatment for children with IM caused by EBV, and symptomatic treatment is usually used to alleviate the disease, and hormone treatment is used for severe patients [4]. The disease is acute and self-limiting. Although the incidence of the disease is not high in children, because EBV can destroy the body's immunity and increase the risk of pathogenic bacterial infections, some of the children may suffer from serious complications such as pneumonia and myocarditis, or even fulminant hepatitis and EBV-associated phagocytosis, which have brought about varying degrees of physical and mental health impacts [5]. Recent studies have shown that people with a history of EBV-IM have a significantly higher risk of developing malignant tumours, especially hematologic and lymphoid tissue malignancies [6]. Therefore, early identification and timely diagnosis and treatment of IM in children are essential. Since the beginning of the twenty-first century, research on IM in children has continued to deepen, and scientists worldwide have paid increasing attention to the pathogenesis, diagnostic modalities, and therapeutic means of IM in children and have made significant progress in this field.

Bibliometrics is the interdisciplinary science of quantitatively analyzing all carriers of knowledge using integrated mathematics, statistics, and linguistics [7]. The concept of bibliometrics was first introduced by Alan Pritchard in 1969 and enriched with infographics by Van Raan in 2004. Since then, this research methodology has been applied progressively to various fields. With the continuous development of global scientific research, the emergence of results, and the increasing amount of literature, summarizing and summarizing the latest progress in the field is a difficult challenge for researchers. Although systematic review can collect, evaluate, and synthesize all the relevant studies on a specific research topic, achieving an organic integration of vertical (timesensitivity) and horizontal (hotspot relevance) for overloaded datasets is challenging. In today's era of big data, bibliometrics can help scientists and clinicians explore the hotspots and frontiers of their research fields, predict future trends, significantly improve their research efficiency, and point the way for future work.

After checking the central global databases, we found that a certain amount of research on IM in children has accumulated in the last 20 years. However, there has yet to be a bibliometric analysis of IM in children. This study aimed to explore the current status, hotspots, and future trends of global research in this field by analyzing published papers on IM in the twenty-first century (2000-2023) using Citespace, VOSviewer, and Bibliometrics software to provide directions and references for future research on IM. Our research objectives are (1) to demonstrate the current status of global research and future development trends in the field of children's IM and to provide directions and references for future IM research; (2) to highlight the current focus of attention through the analysis of hotspots and cutting-edge issues in children's IM research, and to clarify the themes for in-depth research in the future; and (3) to shed light on the developmental problems in the field of children's IM from multiple perspectives, and to propose innovative solutions or suggestions. This will significantly promote the advancement of IM and the publication of results and bless children's health by promoting global medical cooperation.

Materials and methods

Data sources and search strategies

Web of Science Core Collection (WOSCC) is the world's influential multidisciplinary academic literature abstract indexing database, consisting of 10 sub-libraries, containing more than 21,100 globally distributed high-quality academic journals covering more than 250 disciplines, with complete full-text indexing and citation networks for each paper [8]. It is the most commonly used database in the past for bibliometric research [9]. The file format of the data exported from WOSCC complies with the requirements of bibliometric software analysis, and these advantages ensure that comprehensive and precise results can be produced. To prevent errors due to database updates, we searched the WOSCC (SCI-Expanded) database on June 25, 2024, using the following search formula: ts = (("Infectious mononucleosis") AND ("children" OR "infantile" OR "child" OR 'childhood' OR 'pediatric')), yielding a total of 803 documents. The date range was set to 2000-01-01 to 2023-12-31, and 201 documents were deleted. The document type was set to articles (articles) and reviews (reviews), and 32 documents were deleted. The language type was set to English, and 32 documents were deleted. The screening process was carried out by two authors simultaneously and independently retrieving and extracting data. A third author was responsible for verification, significantly avoiding manual bias and ensuring that literature with incomplete conference abstracts, conference papers, editorial materials, lectures, letters, bibliographic information, and duplicates were excluded. Finally, 538 articles were included, exported as plain text files, and saved in "download_***.txt" format. The detailed flow of the search is shown in Fig. 1.

Bibliometric analysis

CiteSpace is a JAVA-based application developed by Dr. ChaomMei Chen of Drexel University (USA) and is well known for its robust co-citation literature analysis [10]. We imported the downloaded literature data into CiteSpace (6.2.R4) with the following settings: period (2000–2023), time node setting [1], link strength (Cosine), link range (within slices), selection criteria (a modified g-index in each slice), network Tailoring Functional Area (Minimum Spanning Tree). Countries, authors, journals, keywords, and references were analyzed using CiteSpace's clustering visualization, biplot overlay, and burst detection capabilities. A team at Leiden University developed VOSviewer. The software uses a visual mapping technique for similarity, which has the advantage of

solid graphical presentation and suitability for large-scale data and text mining [11]. We used VOSviewer version 1.6.19 and ran it by selecting the data type from WOS, setting the counting method to Full counting, adding a word list to clean the data, and then setting the minimum frequency of occurrence of the words. In this study, VOSviewer mainly assisted in the execution of the studies, including co-occurrence analysis of institutions, journals, keywords, and references in three modules: network visualization, overlay visualization, and density visualization. A node on the map of VOSviewer represents a research object, and the size and color of the node denote the number of the objects and the classification of the objects, respectively. Meanwhile, the thickness of the lines between the nodes represents the degree of collaboration or co-citation between the entries. Bibliometrics (https://www.bibliometrix.org), a scientific bibliometrics package based on the R language developed for literature information analysis and visual mapping, was used to visualize the geographical distribution of the research activities in this study, highlighting the different regional contributions and to uncover core journals and

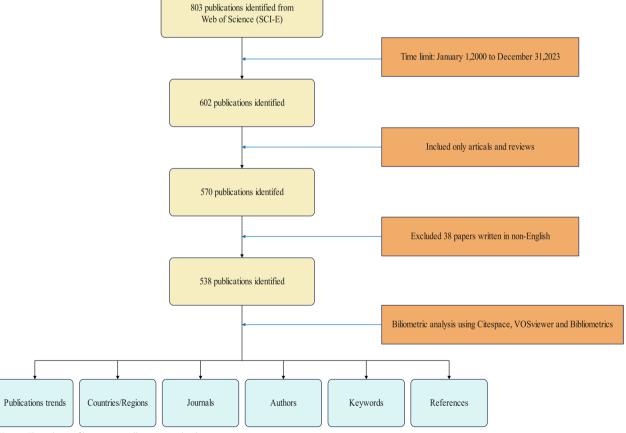


Fig. 1 Flowchart of literature collection and selection

their trends based on Bradford's law. We also obtained impact factors and JCR partitions for journal categories from WOSCC.

Results

Trends in the number of publications

538 authoritative academic papers have been collected in the field of children's IM in the twenty-first century, and the timing of the release of these results is uneven, but there is a pattern. As shown in Fig. 2, in general, the number of papers shows a fluctuating upward trend, and there are four phases in which the number of publications has increased: the first phase (2000-2005) is in a state of steady development; the second phase (2006–2009) shows the trend of "starting down and rapid growth"; the third phase (2010-2016) is prompted by the consolidation of the foundation of the number of publications, and realizes the trend of "rapid growth". The third phase (2010–2016) has achieved a breakthrough in consolidating the base of the number of articles issued; the fourth phase (2017-2023) has realized the reversal from the trough to the peak. The lowest number of publications (n=14) appeared in 2004, 2006, 2007, and 2018, and the highest annual number of publications in the four phases continued to increase, with the highest value appearing in 2023 (n=45) in the fourth phase when the number of publications was 2.6 times higher than that in 2000. The number of citations to papers increased linearly overall, with the rate of increase increasing after 2018.

Analysis of countries/regions and institutions

217 countries/regions and 1752 organizations worldwide have been counted to have conducted research on children's IM in this century. The 21 nodes displayed in Fig. 3A represent different countries. A combination of the number of publications and interconnectedness determines the size of nodes in the updated version of CiteSpace. The connectivity density between the nodes indicates the strength of the cooperative relationship. Purple circles in the outermost layer of nodes with higher centrality indicate they are more cooperative. From 2000 to 2023, the colour changes from grey to red. As can be seen from the figure, the USA (n=155, 26.59%) has the largest node, which has the largest number of publications and extensive cooperation with other countries. ITALY (n = 27, 4.63%) has the sixth most significant number of publications but has a smaller node, suggesting low comprehensive influence.ENGLAND, SWEDEN, and SPAIN are visible in the purple outer circle, which makes their centrality very prominent. Figure 3B presents a map of global postings in children's IM research, with darker colours indicating that they have more postings and red connecting lines representing partnerships in the field. Overall, countries/regions in North America and Europe collaborate closely, with the USA and China making outstanding contributions to the development of pediatric IM. The top 10 countries/regions in terms of the number of publications are shown in Table 1. China (n=95,16.30%) has the second-highest publications after the

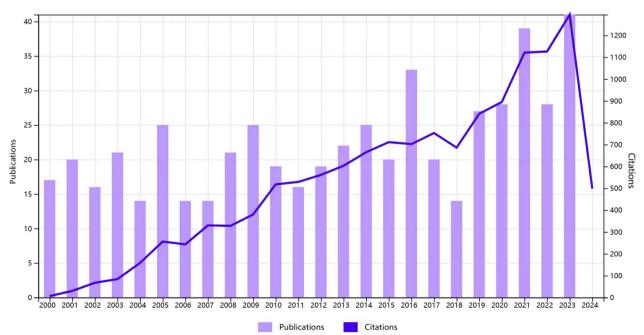


Fig. 2 Annual number of publications and citations for childhood IM studies

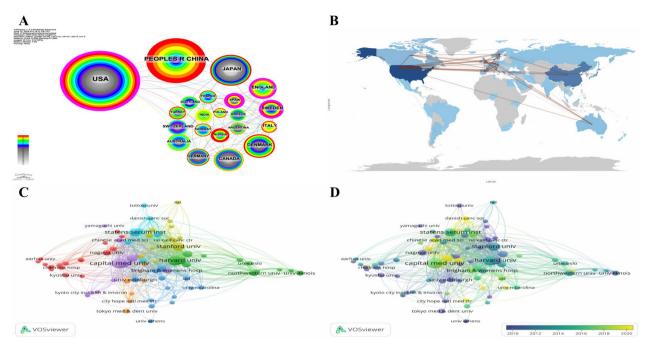


Fig. 3 Visualization of countries/regions and institutions involved in childhood IM research. **A** Distribution of countries/regions involved in childhood IM research. **B** Collaborative map of countries/regions. **C** Cluster analysis of institutions. **D** Timeline visualization of inter-institutional collaboration

Table 1 The 10 countries/regions with the most publications in the field of childhood IM

Rank	Country/Region	Publications	centrality	Citations	Citation per publication
1	USA	155 (26.59%)	0.41	4885	31.52
2	CHINA	95 (16.30%)	0.02	935	9.84
3	JAPAN	53 (9.09%)	0.09	1798	33.92
4	ENGLAND	33 (5.66%)	0.15	1467	44.45
5	SWEDEN	28 (4.80%)	0.13	925	33.04
6	ITALY	27 (4.63%)	0.07	531	19.67
7	DENMARK	22 (3.77%)	0.01	750	34.09
8	CANADA	21 (3.60%)	0.09	676	32.19
9	GERMANY	16 (2.74%)	0.09	689	43.06
10	AUSTRALIA	14 (2.40%)	0.01	411	29.36

USA. However, the centrality is less than 0.1, which indicates that it is dominated by local independent research and has a weaneedsapastronger for international cooperation. JAPAN, DENMARK, CANADA, GERMANY, and AUSTRALIA also share this problem. ENGLAND had the highest mean number of citations (44.45). Table 2 lists the ten institutions that published the most research on pediatric IM, with Capital Medical University (n=21) in the first place, followed by the Karolinska Institute (n=19) and Stanford University (n=14). Half of these ten institutions are from China and the U.S. With 1,136 citations, Harvard University has significantly more

citations than any other institution. It is the most influential research institution in pediatric IM. The highest total link strength is found at Statens Serum Institut (166), an institution with an outstanding international collaborative capacity is outstanding. Figure 3C shows seven main clusters, consisting of institutions with a threshold value greater than or equal to five, where the size of the node represents the number of publications of the institution, each link represents a single partnership, and the different colours of the clusters are used to differentiate the collaboration clusters. We find that the distribution of clusters is characterized by geography, with the

Table 2 The 10 institutions with the most publications in the field of childhood IM

Rank	Institution	Country	Publications	Citations	Total link strength
1	Capital Medical University	China	21	187	53
2	Karolinska Institute	Sweden	19	621	108
3	Stanford University	USA	14	470	122
4	Harvard University	USA	13	1136	87
5	Statens Serum Institut	Denmark	13	316	166
6	Soochow University	China	11	37	47
7	University of Zurich	Switzerland	9	450	30
8	Copenhagen University Hospital	Denmark	8	180	130
9	University of Birmingham	England	8	310	71
10	Zhejiang University	China	8	58	43

Table 3 Top 10 most productive authors and co-cited authors

Rank	Author	Count	Rank	Co-cited author	Citation
1	Hjalgrim, Henrik	12	1	Cohen, Jeffrey, I	130
2	Rostgaard, Klaus	11	2	Kimura, Hiroshi	122
3	Xie, Zhengde	9	3	Hjalgrim, Henrik	114
4	Chang, Ellen, T	6	4	Balfour, Henry, H	95
5	Huang, Linlin	6	5	SUMAYA, CV	87
6	Katz, Ben, Z	6	6	Imashuku, Shinsaku	80
7	Kimura, Hiroshi	6	7	Ascherio, Alberto	64
8	Shi, Ting	6	8	Brook, I	64
9	Taylor, Renee	6	9	Dunmire, Saman- tha, K	63
10	Ai, Junhong	5	10	Glaser, Sally, L	62

institutions at the top of the list of publications being central to the main clusters. Harvard University in the green cluster, Capital Medical University in the purple cluster, Statens Serum Institut in the sky blue cluster, and Stanford University in the yellow cluster communicate closely and serve as bridges between clusters. Fewer institutions are involved in pediatric IM research today than in the past, and those with a high volume of publications have not always maintained their research enthusiasm, with institutions such as the Danish Cancer Institute standing out in the post-2020 period (Fig. 3D).

Analysis of authors and co-cited authors

2613 authors have been involved in research on IM in children in the twenty-first century. Hjalgrim, Henrik has published the most articles (n=12), followed by Rostgaard, Klaus (11 articles) and Xie, Zhengde (9 articles), and the authors ranked 4th to 10th in terms of the number of publications are shown in Table 3. The table also lists the ten authors with the highest number of citations, with Cohen, Jeffrey, and I at the top of the list with 130 citations and Kimura, Hiroshi (n=122) and Hjalgrim,

Henrik (n = 114) with more than 100 citations. Figure 4A, B show the authors' collaborations and authors' simultaneous citation degrees, respectively. The difference in the colour of the circle compositions in the nodes reflects the authors' contributions to the field of children's IM in different years of the century, with the colour corresponding to the year illustrated in the lower left of the figure. In terms of authorship, it is clear that Hjalgrim, Henrik and, Rostgaard, Klaus have had a prominent research impact, with a continuity in the research timeline spanning almost two decades, and that the authors with whom they have worked closely have not had any new children's IM results published in recent years. We also identified four significant collaborations: first, the cluster represented by Xu, Yin; second, the cluster represented by Xie, Zhengde; third, the cluster represented by Tian, Jianmei; and fourth, the cluster represented by Zhou, Weifang. They are influential new faces in the field, and after investigation, it is found that they are mainly from hospitals or research institutes in China. Figure 4B shows that the co-cited authors are closely connected, and emerging and past authors are cited simultaneously, presenting a blossoming academic landscape. In addition to the top three authors in terms of citations, the node where Ascherio Alberto is located has a purple outer circle, and they are considered to be authoritative scholars in the field of pediatric IM.

Analysis of core journals

Since the beginning of the twenty-first century, more than 300 journals in the Science Citation Index have published articles in pediatric IM. Figure 5A filters out 32 core journals in the field by Bradford's law by ranking the journals in decreasing order according to how many specialized papers they publish, and all of these journals have a publication volume greater than or equal to 3. Due to the large number of journals with a publication volume of less

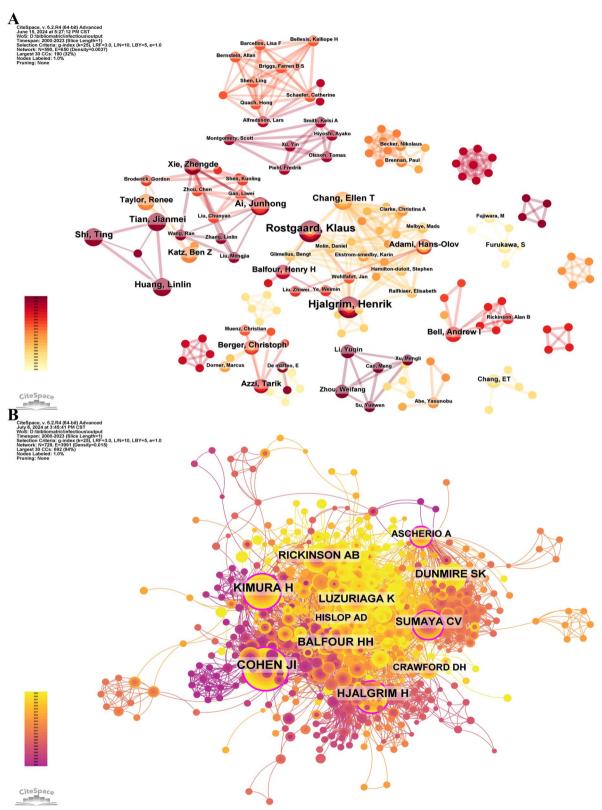


Fig. 4 Network of authors and co-cited authors of childhood IM publications. A Author network based on co-citation analysis. B Co-cited author network based on co-citation analysis

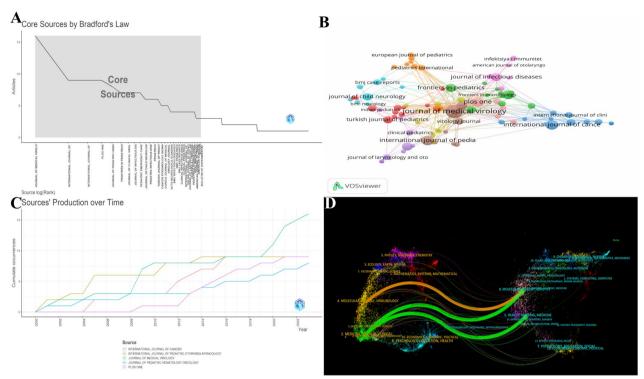


Fig. 5 Analysis of Children's IM Journals. A Core journals for childhood IM research based on the Law of Bradford. B VOSviewer web maps for journals. C Growth of the five highest yielding journals for childhood IM research in the twenty-first century. D The dual-map overlay of journals

than 5, in Table 4, we focus on the top 10 journals, and we find that the JOURNAL OF MEDICAL VIROLOGY has published the most papers [16] and has the highest IF, which is a strong promoter of pediatric IM research. INTERNATIONAL JOURNAL OF CANCER, PLOS ONE and JOURNAL OF INFECTIOUS DISEASES are all located in the JCR1 region of the corresponding journal category, which provides a solid platform for the dissemination of the results of pediatric IM. Papers published in JOURNAL OF INFECTIOUS DISEASES had the highest

number of citations (n=520), followed by PLOS ONE (n=516). The top five journals with the highest number of publications are tracked over time in Fig. 5C, and their annual publications over the past 23 years are not homogeneous but have plateaued (a period with no increase in publications) and have occurred separately which ensures the sustainability of the global research outputs. JOURNAL OF MEDICAL VIROLOGY and JOURNAL OF PEDIATRIC HEMATOLOGY ONCOLOGY have continuously increased in total publications in recent

 Table 4
 Information on the top 10 journals in terms of publications

Rank	Journal	Publication	IF(2023)	JCR	Citations
1	JOURNAL OF MEDICAL VIROLOGY	16	6.8	Q1	271
2	INTERNATIONAL JOURNAL OF CANCER	9	5.7	Q1	175
3	INTERNATIONAL JOURNAL OF PEDIATRIC OTORHINOLARYN-GOLOGY	9	1.2	Q3	154
4	PLOS ONE	9	2.9	Q1	516
5	JOURNAL OF PEDIATRIC HEMATOLOGY ONCOLOGY	8	0.9	Q4	47
6	FRONTIERS IN PEDIATRICS	7	2.1	Q2	31
7	JOURNAL OF CLINICAL VIROLOGY	7	4	Q2	350
8	JOURNAL OF INFECTIOUS DISEASES	7	5	Q1	520
9	PEDIATRIC EMERGENCY CARE	7	1.2	Q3	49
10	JOURNAL OF CHILD NEUROLOGY	6	2	Q2	183

years. The distribution of journal clusters (Fig. 5B) shows a total of 10 significant clusters, which are more tightly connected, suggesting that there is a correlation of citations between journals and that mutual citations contribute to the growth of the field. Figure 5D shows a two-map overlay of journals, with the orange path indicating that studies published in "Molecular, Biology, Immunology" journals cite more from "Molecular, Biology, Genetics", and the green path indicating that studies published in "Drugs, Medicine, Clinical" journals cite more from "Molecular, Biology, Genetics".

Analysis of keywords and research areas

Keywords are the basis for mining hot and cutting-edge issues in the research field, and we analyzed the keywords from different aspects. Table 5 lists the 20 keywords that appeared most frequently, and the top 8 keywords were all related to the population and diseases set in the study (e.g., children, Epstein-Barr virus infectious mononucleosis, etc.), which verified the accuracy of the literature search. In addition to this, diagnosis (n=44), antibody (n=40) and epidemiology (n=35) were the keywords with the relatively highest frequency. The cluster analysis is visualized in Fig. 6A, where it can be seen that the keywords formed ten major clusters, mainly including #0 Epstein-Barr virus, #1 plasma, #2 childhood social environment, #3 chronic fatigue, #4 multiple sclerosis, #5 tonsillitis, #6 hemophagocytic lymphohistiocytosis, #7 epstein barr virus, #8 sequencing, #9 cervical lymphadenopathy. They are a high-level summary of the research direction on childhood IM in the twenty-first century. The 25 keywords with the highest intensity of cited outbreaks were sorted according to the time of outbreaks (Fig. 6B), and the keyword with the highest intensity was epstein barr virus (5.38), while those with an intensity greater than 4 were multiple sclerosis (4.16), risk (4.61), and children (4.7). The keywords that have appeared in outbreaks in the last 5 years are multiple sclerosis, natural killer cells, epstein barr virus and clinical characteristics. childhood social environment, risk factors, prevalent, and lymphoma have the longest time span of 6 years. VOSviewer plotted the keywords presented on the density map (Fig. 6B), and the brighter the colour of the area where the keyword is located, the higher the frequency of its appearance in the article, from which we found that covid-19 gene, and cd4(+), which are the concerns of the medical community, also appeared in this area. Figure 6D categorizes the research areas of pediatric IM according to the disciplines to which the keywords belong. Among them, there were 132 papers (24.5%) in the direction of paediatrics, 55 papers (10.2%) in the direction of oncology, and 53 papers (9.8%) in the direction of immunology.

Analysis of references

The results of the citation burst detection analysis are shown in Fig. 7A, where we can see that these 25 citations were published from 1999 to 2021, which is very close to the publication time of the literature included in this study, reflecting the immediacy of the study. The intensity of citation bursts is concentrated between 9.24 and 3.4, among which "Dunmire SK, 2018, J CLIN VIROL, V102, P84, https://doi.org/10.1016/j.jcv.2018.03. 001" has the most robust burst, and the time of bursting is the latest. A total of seven papers exploded in the last three years and continue until 2023, which is a hot reference for research. In recent years, a total of more than 13,000 documents have been cited by child IM research; we analyzed the cited references and plotted their citation relationships as shown in Fig. 6B, from which we can see that the ten most cited papers are scattered in four clusters and are essential components of the clusters and that there exists a solid academic connection among them. The information on the ten most cited papers is shown in Table 6 (Supplementary file). Among them,

Table 5 Top 20 keywords related to childhood IM

Rank	Keyword	Counts	Rank	Keyword	Counts
1	Children	179	11	Epidemiology	35
2	Epstein–Barr virus	179	12	Childhood	34
3	Infectious mononucleosis	177	13	Lymphoma	31
4	Infectious-mononucleosis	139	14	Multiple sclerosis	29
5	Epstein-Barr-virus	116	15	Infection	27
6	EBV	66	16	Risk	27
7	Disease	64	17	Expression	26
8	Mononucleosis	51	18	Hemophagocytic lymphohis- tiocytosis	26
9	Diagnosis	44	19	EBV infection	24
10	Antibody	40	20	Prevalence	23

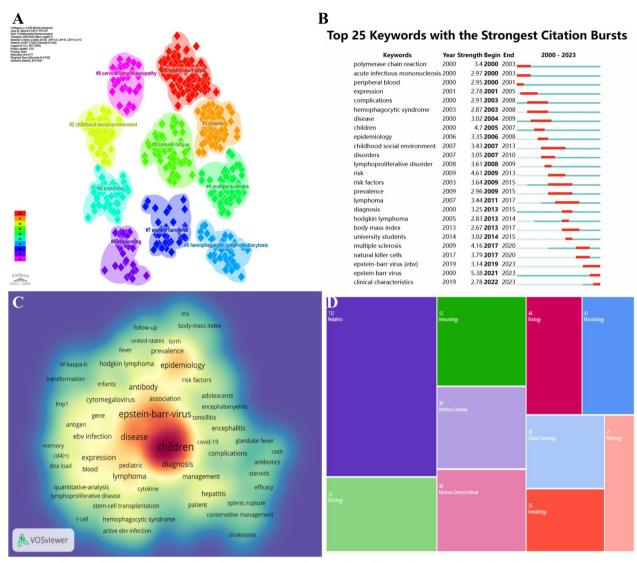


Fig. 6 Visualization of childhood IM keywords and research areas. A Cluster analysis of keywords. B Top 25 keywords with the highest number of citation outbreaks. C Density map of keywords. D Categories of research areas involved in childhood IM

the paper entitled "Multiple sclerosis: risk factors, prodromes, and potential causal pathways (n=368) was the most cited.

Discussion

The World Health Organization, in its International Classification of Diseases, classifies IM into four subcategories: EBV-related IM, CMV-related IM, other IM, and unspecified IM. When defining IM diseases in many studies, the four types are often lumped together as the same, indicating only that they are due to different etiologies [12]. We found the most significant proportion of EBV-IM-related studies in the pediatric

population by analyzing the primary keyword sources, which is consistent with the recognition that EBV is the most predominant aetiology of IM in children. It has been shown that EBV-IM is positively associated with multiple sclerosis (MS), while the opposite is true for CMV-IM [13]. Although more than 90% of the world's population has been infected with EBV, only a tiny percentage develops IM, especially in the pediatric population aged less than 5 years, where IM usually presents atypically. The insufficient number of confirmed cases in children has led to limitations in research, but the potential morbidity of the disease is enormous. A substantially increased risk of depression later in life has also been reported in children or adolescents with IM

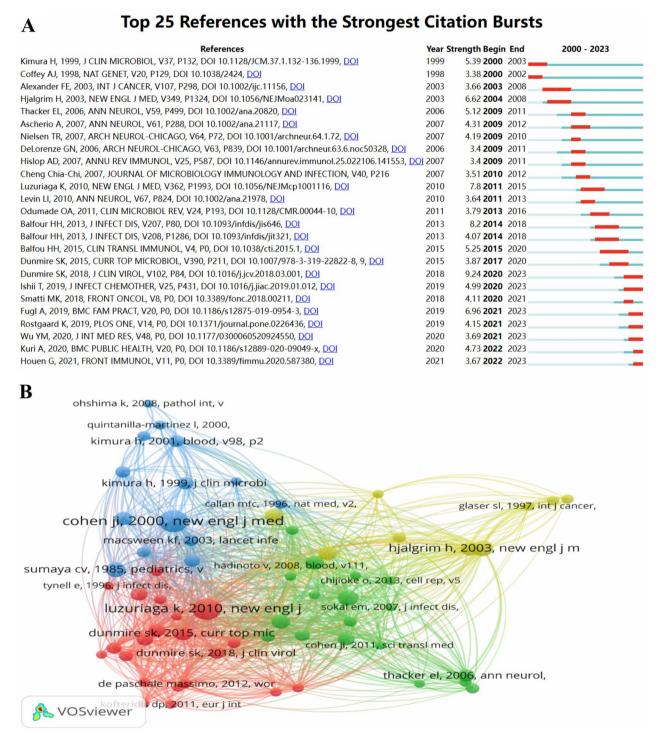


Fig. 7 Visualization of cited literature. A Top 20 citations with the highest number of citation outbreaks. B Visualization of co-cited literature

[14]. Thus, full recognition and timely intervention for IM are essential for the health of the world's children.

Into the twenty-first century, the number of studies on children's IM has generally shown an upward trend. The prospects for continued exploration are promising. Although there have been a couple of drops in annual publications, this has yet to be sustained. In the subsequent period, the growth trend will stimulate new growth. This phenomenon suggests that the years of low publications in the field are not the result of a decrease

in researchers' attention to children's IM and that there are hidden extraneous factors or serendipitous. An average increase of 6.2 papers per year from 2018 onwards is expected in Phase IV, with a breakthrough expected in 2024. The number of citations of related studies changes significantly. It is mainly independent of the number of publications, indicating that the research results are widely recognized and referenced by scholars worldwide, not limited to IM in children. Looking back at the past 23 years, the 538 papers are slightly less than the research results in other fields, and our analysis suggests that this may be due to the limitations of the pediatric population and the fact that children are usually mildly symptomatic when they have primary EBV infection. With further research and global collaboration, the field of pediatric IM is poised to achieve more extraordinary results.

Overall, the countries/regions involved in children's IM research are unevenly distributed globally, mainly concentrated in North America, Europe and East Asia, most of which are developed regions. Among them, the USA is the leading country in the development of child IM, ranking first in the number of publications and citations. China has accumulated enough results, but its influence and ability to cooperate globally still need improvement, so it must continuously explore new academic development paths. England has the highest citation rate per publication on average, and these influential results have contributed to the continual deepening of the research. At present, a new development pattern of "three centers and one network" has been formed. The "three centers" refer to the three countries (USA, CHINA and JAPAN) that contribute the most to pediatric IM, and the "one network" refers to the collaborative platform composed of countries with solid cooperation capabilities (USA, ENGLAND, SWEDEN and SPAIN), which should communicate and cooperate, and endeavour to gradually build a more extensive and more influential research network in the future research. Capital Medical University has the most significant number of publications among the research institutions. However, the number of citations and total link strength is relatively weak, so it is necessary to continue strengthening the ability to collaborate while ensuring the output of results. Harvard University has the most significant citations and a global academic impact. Statens Serum Institut has the most muscular total link strength and is a model of inter-institutional cooperation; the Danish Cancer Institute, as a potential new research institution, should take the initiative to cooperate with the University of Illinois while continuously improving its research capacity; the University of Edinburgh and other former major pediatric IM research institutions to promote the publication and translation of new results.

We also note that despite the large number of papers published in children's IM in some countries (e.g., China), the citation rate and impact are low. Through a further review of the literature, we synthesized this phenomenon in three ways. In the first place, studies in China have mainly focused on the epidemiological characteristics, diagnostic modalities, and immune response mechanisms of local pediatric populations. These studies usually focus on clinical observations and often lack in-depth collaboration with international organizations, making their findings less frequently cited by international scholars. In contrast, research in the United States and Europe tends to have stronger international and interdisciplinary cooperation, and research results are more likely to be recognized globally. Second, although China has a more significant number of studies in the field of children's IM, due to the insufficient allocation of research funds and the relative lack of academic resources, many of the research results have not been of outstanding quality, have failed to be published in top international journals, and have focused mainly on solutions to local problems, which have failed to be disseminated and cited sufficiently in an international perspective. However, the locality is of great practical significance. Finally, we analyzed the impact of clinical practice on IM research in different regions. In the United States and Europe, research has focused on the immune mechanisms of IM, the relevance of multiple sclerosis, and the long-term health effects after EBV infection, and these findings are more globally relevant. In contrast, studies in China tend to focus more on early diagnosis, optimization of treatment regimens, and local epidemiological characteristics, which provide important data support for Chinese children's health but have not yet developed a broad international impact. In the future, researchers should strengthen international cooperation and enhance the internationalization of their papers, with an eye on public health issues of common global concern to protect the health of all humanity.

Finding that although research institutions from lowand middle-income countries are deficient in IM research output, they also contribute positively to the development of the discipline, we further explored institutions in representative regions (e.g., Africa and South America). The African region has a limited number of papers that provide valuable insights into the local epidemiology and immunologic mechanisms of IM, with research focusing more on the long-term health effects of EBV-associated disease and differences in immune responses in pediatric populations [15, 16]. The South American region has seen a progressive growth in the literature, especially regarding epidemiologic studies and therapeutic strategies. Among them, Brazilian studies provide an in-depth practical discussion of the diagnosis, treatment strategies, and management of IM complications in children from a developing country's perspective [17, 18]. The Argentinean institutions are more interested in EBV-related tumors (lymphomas) [19, 20]. They all focus on effective disease management in resource-limited settings, which provides a unique perspective on understanding IM in different socioeconomic contexts.

With the initial formation of author clusters in children's IM, we find that the researchers within the clusters are distinctly geographic and that the links between clusters need to be strengthened. Clusters of today's lead and former lead authors occupy a central position. Conversely, clusters in which the two types of authors are not combined are more minor, suggesting the importance of scholarly legacy. Hjalgrim, Henrik and Rostgaard, Klaus, the authors with the highest number of publications and a significant force in research on pediatric IM, have jointly commented on a recent Goldacre published review of a study that provides insight into the EBV-MS risk correlation and demonstrates the observation of an increased risk of MS in individuals diagnosed with IM but is unclear as to whether the best predictor of MS after IM in adolescents is late primary EBV infection or IM, and needs to be validated at a later date [21]. They also explored the relationship between antimicrobial use, childcare attendance, and IM risk based on a Danish pediatric population [22, 23]. The co-cited authors are closely related and form a scholarly consortium, with Cohen, Jeffrey, and I being the most influential authors in the consortium, who have investigated the fusion mechanism of EBV and innovated a potential therapeutic antibody for EBV disease, laying the foundation for vaccine and drug development [24-26]. Kimura, Hiroshi ranked second in the number of citations and tied for fourth in the number of publications after Hjalgrim, Henrik. Kimura, Hiroshi [27, 28] analyzed EBV mainly regarding gene expression and cellular mechanisms. The emergence of lead authors and co-cited authors provides a strong talent support in the field of pediatric IM, and how to strengthen the efficient collaboration among researchers is also a topic to be tackled in the future, aiming at a sustainable guarantee for the progress of the discipline.

The number of core journals obtained from Bradford's law is large. However, we found that some of the journals have a low number of publications in the field and need to be more suitable for core journals in the true sense of the word. We analyzed the reasons for this and concluded that this may be related to the overall low number of publications and the high number of journals publishing the same number of papers. We designated new core journals by combining the distribution of journal clusters: INTERNATIONAL JOURNAL OF CANCER in the blue cluster, FRONTIERS IN PEDIATRIC in the green cluster,

JOURNAL OF MEDICAL VIROLOGY in the brown cluster, and JOURNAL OF INFECTIOUS DISEASES in the pink cluster, and PLOS ONE in the light pink cluster. These journals are not only at the top in the number of articles published but are also the centres of significant clusters with high impact. The disciplinary attributes of the five journals are not uniform, and they should play to their strengths by reinforcing the scholarly status of pediatric IM while innovating and actively engaging with molecular, biology, immunology, Genetics, Health, Nursing and Pharmacology to realize leapfrog development.

Collating key cited literature in pediatric IM will effectively contribute to future research hotspot mining and critical problem-tackling. Dunmire, SK conducted a systematic review of EBV in 2018, summarizing various aspects such as prevalence, transmission routes, incubation period, aetiology, diagnosis, and treatment, and pointing out the need to strengthen the study of epidemiology and pathogenesis, with a particular emphasis on paying more attention to pediatric EBV infection [29]. As a cited literature with remarkable explosive power and time of outbreak, this paper will be more referenced and studied in the future as a cornerstone for developing the discipline. Ramagopalan et al. [30] published a paper in the prestigious journal LANCET NEUROLOGY with the highest total number of citations. It provides an overview of multiple sclerosis, especially describing its risk factors, prodromal symptoms, and potential pathogenic pathways. In recent years, many studies [13, 31, 32] have confirmed that EBV-IM is associated with an increased risk of multiple sclerosis, so we hypothesized that this most co-cited paper has also been used to explore the relationship between IM and multiple sclerosis in children. Thacker, EL, carried out a systematic evaluation and meta-analysis. This study became the second most cocited paper, with the findings suggesting that in the adolescent population, EBV-IM is a risk factor for MS [33]. Based on the above analysis, we believe that the theme of the cited literature is not primarily the IM disease itself, which suggests that both the factors that influence the pathogenesis of IM and the diseases that IM affects are aspects of research into the field.

Keywords are the most direct reflection of the topic and content of the paper, and they are important clues for finding the hotspots and frontiers of research. This study's disciplinary distribution of related literature mainly focuses on paediatrics, oncology, immunology, infectious diseases and internal medicine. Although some of these disciplines do not accurately reflect the essential attributes and research areas of IM, they fully demonstrate the importance of various disciplines and the trend of multidisciplinary cross-development of IM. We should deeply summarize the correlation between IM and

tumours, explore the immune dysregulation mechanism of IM, and focus on clinical research in conjunction with the children's population so as to move forward to prevent and treat IM. Combining the frequency (density) of keyword appearances, keyword clustering, and keyword outbreaks, we summarize the research hotspots in the field of IM in children in the twenty-first century, including the characteristics of diagnosis and assessment of IM, the association of IM with other diseases, and interventions for IM. The frontier of research is the pathogenesis of IM due to EBV. In the clinic, we have found that children with IM may not have all of the typical symptoms, and haematological parameters are more accurate than symptoms and signs; looking for problems that characterize IM will help to identify the disease in time and increase the accuracy and relevance of the diagnosis. Although some studies [34] have characterized the immune events of EBV infection in children with acute IM and have shown a substantial expansion of CD8+T cells with downregulation of CD62L, upregulation of PD-1 and CTLA-4 on T cells, enhanced production of granzyme B, and impaired secretion of IFN-y, enrichment analyses of EBV-IM specific protein pathways and processes have shown that the complement system is the most enriched group of up-regulated proteins in the disease [35]. A study [36] based on a Chinese pediatric population characterized the epidemiology of IM, with the incidence of the disease increasing during the summerautumn transition (July-September) and decreasing during the winter-spring transition (January-February), and bronchiolitis/pneumonia and hepatic dysfunction being the two most common complications. 40%-80% of children with IM develop liver injury, which can progress to liver failure, one of the leading causes of death from IM.18 In addition [37], IM is a significant cause of death in children with chronic illness—one of the leading causes of death in IM. Real-time monitoring of adenosine deaminase, high mean platelet volume to platelet count ratio, and percentage of HLA-DR+CD8(+) T cells assesses IM severity in children and predicts liver injury[38-40]. A related study in the UK, on the other hand, found that whiteness, lower BMI, and never having smoked were exposure factors for IM, and these exposures interacted with each other [41]. Serologic antibody and viral nucleic acid testing are currently viable methods for diagnosing EBV-IM in children, but sensitivity varies by age; plasma EBV-DNA testing has the highest diagnostic value in children < 6 years of age, especially < 3 Years of age should be used early with EBV antibody and EBV nucleic acid testing. Peripheral lymphocyte testing and plasma EBV-DNA testing are appropriate for Peripheral lymphocyte testing and plasma EBV-DNA testing, which are indicated within seven days of disease, after

which VCA-IgG affinity testing is more appropriate [42]. IM often involves other organs during the pathogenesis, especially in the pediatric population, and can cause various complications worthy of our knowledge and attention. It will also help us take appropriate therapeutic measures to intervene effectively. Usually, EBV infection is considered to be the cause of multiple sclerosis. However, studies have shown that the prevalence of MS in patients with IM is three times higher than in the general population, with strong associations in long intervals of more than 5 years [32]. Myalgic encephalomyelitis/ chronic fatigue syndrome (ME/CFS) after EBV-IM is a severely debilitating disease with a delayed clinical diagnosis that has a more significant impact on physical functioning and health-related quality of life in adolescent patients [43]. Eighty per cent of patients with splenic rupture or infarction present with symptoms of IM before 3 weeks of onset [44]. The results of a cohort study showed a significant association between IM and increased incidence of Crohn's disease, and based on the data, it is hypothesized that EBV is involved in the development of Crohn's disease [45]. In all age groups, EBV-IM is associated with hematologic malignancies, especially with an increased risk 2 years after IM exposure, and long-term follow-up of children with IM is also essential [46]. In addition to common complications and isolated individual cases, some studies have suggested that IM in children is also associated with nonalcoholic fatty liver disease [47], acute noncalculous cholecystitis [48], and tracheal obstruction [49]. However, the populations in these studies were geographically limited and will need to be validated later by global multicenter studies with large samples. There are no specific drugs for IM, and patients are generally advised to reduce activity and bed rest for 8 weeks or when splenomegaly is present. Scientists are searching for effective interventions to safeguard children's lives and health through various clinical trials. One study systematically evaluated antiviral drugs for IM and found that clinical recovery time was reduced by an average of 5 days after treatment, lymph node swelling duration was reduced by an average of 9 days, and viral shedding was inhibited during treatment [50]. However, the quality of the evidence was rated as very low in all cases, and this therapy is controversial. There have also been systematic evaluations of clinical studies of steroids for the treatment of this disease, with the results suggesting only the use of steroids to control the symptoms of IM, with side effects and complications requiring more long-term studies [51]. Based on the understanding that IM is associated with anaerobic bacterial infections, metronidazole has also been used clinically to reduce the length of hospitalization for severe IM significantly [52]. The excellent efficacy of Chinese herbs

in treating IM in children has also been confirmed. Herbs have the efficacy of clearing heat, removing toxins, activating blood circulation, and removing blood stasis, which is more effective and safer than other therapies and is an important therapeutic approach for future breakthroughs [53]. In the presence of comorbidities, the application of antibiotics is unavoidable, in which the administration of aminopenicillins may increase the risk of skin rashes in children with IM. However, amoxicillin is not such a risk, and clinicians should choose to use it after scientific deliberation in selecting the medication to be used [54]. The mechanism of IM due to EBV is currently inexact, and researchers have been exploring it continuously. EBV undergoes two cycles of production and lysis and dormant latent two cycles; after entering from the mouth, it first invades the epithelial cells at the back of the throat, so the tonsils, cervical lymph nodes, and trachea will be seen to be involved. Panikkar et al. [55] demonstrated a significant loss of circulating myeloid and plasmacytoid dendritic cells during acute IM regarding inflammatory cytokines and T-cell homeostasis. This alteration correlated with clinical severity. Acute IM symptoms coincide with the rapid destruction of memory B cells by CTLIEs upon entry into viral replication. Fifty per cent of mBLats may be destroyed within 1 week of peak infection, which leads to massive and continuous deposition of cellular and viral antigens into the system, a result that causes long-term damage to the immune system while also serving as a predisposing factor for IM-associated disease [12]. The dynamic expression profiles of viral and cellular miRNAs also provide an essential basis for mechanism exploration [56]. Of course, there are many other studies on the mechanisms of IM in children worldwide, and we have only scrutinized the representative results. The complete results need to be reviewed comprehensively by writing a review.

We analyzed high-frequency keywords and found that MS dominates IM research. However, the relationship between the two deserves to be further recognized and summarized by researchers. MS is a chronic disease of the central nervous system that can lead to immunemediated demyelination and axonal degeneration and, ultimately, progressive neurological disability [57]. In Western countries, more than 90% of people are infected with EBV during their lifetime, and EBV triggers IM and may be a prerequisite for the development of autoimmune diseases. A large German cohort study of patients with early MS demonstrated that EBV infection may lead to a breakdown of the immune tolerance network, which promotes the onset of MS [58]. Prospective long-term studies have found that high IgG titers against EB nuclear antigen (EBNA)-1 or EBNA complexes are associated with an increased risk of subsequent MS [59]. Patients with anti-EBNA complexes≥320 and EBNA complex IgG titers≥320 had a 30-fold greater risk of developing MS than patients with titers < 20 [60]. From the pathophysiological basis of autoimmune diseases, the association between MS and IM can be elucidated by molecular modeling. Molecular mimicry is based on a cellular or humoral immune response against an infectious agent that is misdirected due to a reaction with a self-antigen [61]. Another theory suggests that EBV may be latent in autoreactive B lymphocytes, which in turn induce autoreactive T cells that act as antigen-presenting cells, thereby ultimately triggering organ damage in autoimmune diseases such as The study by Lanz et al. [62] combines both theories by extracting a cerebrospinal fluid-derived mAb targeting EBNA1AA386-405 that revealed a molecular mimicry of GlialCAM. This cross-reactivity represents a broader phenomenon in MS patients, as plasma primitive cells in the cerebrospinal fluid of MS patients produce antibodies against multiple GliaICAM epitopes. This offers a potential approach to the treatment of MS.

We summarize our findings: EBV-related IM studies in the pediatric population have received increasing attention from scientists in recent years. These studies have generally standardized and updated the clinical manifestations, pathogenesis, and complications of IM. Understanding the epidemiologic characteristics of IM in children with weakened immune function in different regions can help clinicians diagnose and recognize the disease more accurately. The typical symptoms of IM, such as fever, lymph node enlargement, and pharyngolaryngitis, are similar to those of other upper respiratory tract infections. The clarity of clinical manifestations can provide key clues to the clinical diagnosis of IM, especially in areas with a high prevalence of the disease, helping clinicians to confirm the diagnosis quickly and reduce the chance of misdiagnosis. How to manage IM effectively is particularly important in resource-limited settings. With a comprehensive understanding of the clinical manifestations and complications of IM, physicians can better recognize symptoms and avoid over-treatment while relying on symptoms in advance to make initial judgments and take advantage of prevention without sophisticated diagnostic equipment. In response to the local spectrum of common diseases, IM research can help prioritize treatment options and improve the efficiency of diagnosis and treatment. An indepth understanding of the global distribution and clinical characteristics of IM can help prioritize the disease in the clinic and achieve better treatment options in different resource settings.

The research on IM has initially shown interdisciplinary cooperation, and it is crucial to take advantage of multidisciplinary integration in future research on pediatric IM and its related diseases (e.g., autoimmune diseases and malignant tumors). In this regard, we propose the following suggestions to help the development of the discipline: First, establish a joint research project among experts in immunology, oncology, and pediatrics to jointly evaluate the immune response, pathogenesis, and interventions of IM in children at different ages, through clinical trials and laboratory data analysis. Specifically, a long-term tracking program targeting changes in children's immune systems after EBV infection could be established, especially the incidence of malignancies related to the blood and lymphatic systems. Second, a unique global data-sharing platform should be created to integrate clinical records, experimental samples, and research results in the fields of immunology, oncology, and pediatrics so that regions with insufficient medical resources can also have the opportunity to participate in scientific research and comprehensively promote compelling diagnostic and treatment experiences, in order to strengthen the breadth and depth of interdisciplinary research. Thirdly, academic conferences and seminars are regularly organized with leading experts and young scholars in the fields of combined immunology, oncology, and pediatrics, inviting emerging scientists to share research progress and discuss the potential links between IM and autoimmune diseases and malignant tumors, thereby promoting collaboration and exchange in the academic community and the practical application of interdisciplinary research.

The development of pediatric IM can only be achieved with the joint efforts of scientists from all over the world, and the construction of the collaboration model is of landmark significance in developing the discipline. Our team has previously proposed the "breakthrough-improvement-cultivation" model [63] and the "country-institution-journal" model [64] based on the characteristics of different research fields, enriching the connotation of global academic cooperation. In this study, after rational analysis and judgment, we propose a new model of cooperation in the field of children's IM, "increasing quantity-improving quality-integrating": (i) "increasing quantity" is to steadily increase the number of annual publications in the field of children's IM in all aspects, to make an excellent theoretical foundation for the development of the discipline. The United States, China, and other major output countries provide scientific research for their research institutions and scientists to provide scientific research support and technical support, the use of national platforms to organize the central domestic IM research institutions for cooperation and exchange through the strong with the weak way to expand the research clusters, enhance the scientific research team's scientific research capabilities, and increase the output of research results. Authoritative international journals can encourage more researchers to participate actively in related research by adding columns on pediatric IM, expert appointments, and rapid review of manuscripts. The World Medical Organization should coordinate the development of research plans for pediatric IM, deploy research tasks that meet national conditions, and provide targeted financial support so that every country has the conditions to carry out clinical and basic research on pediatric IM. (ii) "improving quality" means that research results in pediatric IM should achieve leapfrog progress in terms of quality to promote more breakthroughs in the field, and primary research institutions such as Capital Medical University and the Karolinska Institute should build a research platform to conduct multi-centre, large-sample clinical trials. The primary research institutions, such as Capital Medical University and Karolinska Institute, should build a research platform together, conduct multi-centre and large-sample clinical trials, and formulate global diagnosis and treatment guidelines by taking into account the characteristics of IM in different regions to promote the translation of high-quality results. Lead authors and cocited authors from different countries should discuss the key issues promptly and categorize the research difficulties, hotspots, and research priorities in pediatric IM so that other researchers can keep abreast of and dynamically adjust their research directions. Authoritative journals have the mission to disseminate excellent results. High-quality journals should hold the quality gate, continuously expand authoritative scholars in pediatric IM to join the reviewers' team, take the initiative to undertake the task of publishing on the guidelines and consensus and strengthen the communication in terms of manuscript allocation, publishing experience and daily management to ensure quality improvement from the root. (iii) "integration" includes cross-disciplinary integration and integration of theoretical results. In our study, we found that publications on pediatric IM cover a wide range of research areas. While studying the IM disease, we should continue to expand the study of IM complications and IM-like diseases, which requires comprehensive cooperation between research disciplines. Through integrating research data and professional knowledge and fusion, we can achieve a unified understanding of different diseases, which will vigorously promote the development of the cause of human health. Different scholars have different understandings of the pathogenesis and treatment of IM in children, and they should also turn inconsistency into unity through clinical practice and scientific research, screen the optimal solutions in the results, and continue to innovate in the fusion to promote the sustainable development of IM in children.

Advantages and limitations

This is the world's first bibliometric analysis of highquality papers published in children's IM. Compared with reviews and meta-analysis, it can objectively and comprehensively summarize hot topics and cuttingedge directions about IM and plan the future research and development landscape by analyzing basic information such as countries/regions, institutions, authors, and journals. This study also has shortcomings: limited by the nature of the analysis software; we only included papers from the WOSCC database, which may result in accurate but incomplete data. The number of papers included was limited because only 'article' and 'review' type studies were retained in English. Due to the time lag between publication and inclusion in the database, some recently published articles may not have been included. However, these limitations do not detract from the critical role of bibliometrics in exploring research hotspots and prospects in pediatric IM.

Conclusion

This study used bibliometrics to analyze and visualize publications related to children's IM. The study's results objectively show that the number of publications on pediatric IM research has shown four stages of development in the twenty-first century, with a clear growth trend, especially from 2017 to the present. The United States has the highest number of published journals, and Capital Medical University has emerged as the most productive institution. Hjalgrim, Henri is the most contributing author in the field. JOURNAL OF MEDI-CAL VIROLOGY is the journal with the highest output. Research hotspots include diagnosis and assessment of IM characteristics, association of IM with other diseases, and interventions for IM. Recent research trends indicate that the pathogenesis of IM due to EBV is receiving increasing attention, and future studies should further explore new mechanisms and effective therapies for EBV-IM. There is no close collaboration between countries, institutions, and authors, and further interconnections must be strengthened. The research results between regions are not balanced, and it is necessary to learn from each other and complement each other's strengths and weaknesses according to their actual needs. The multidisciplinary integration and communication are not deep, and we need to explore new research-oriented methods in clinical practice. Together, we can promote the highquality development of pediatric IM.

Abbreviations

IM Infectious mononucleosisEBV Epstein–Barr virusWOSCC Web of Science Core Collection

MS Multiple sclerosis

Supplementary Information

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Additional file 1.

Author contributions

CZJ designed the study and drafted the manuscript. DJJ and PYL searched strategy. CZJ and WJJ completed the statistical analysis. XLM reviewed and modified the manuscript. All authors contributed to the article and approved the submitted version.

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Availability of data and materials

The authors confirm that the data supporting the findings of this study are available within the article and its supplementary materials.

Declarations

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Competing interests

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