Research Article

Trends in *Plasmodium vivax* Vaccine Development Research: A Pubmed-based Bibliometric Analysis (2001- 2025)

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Abstract

Genetic diversity, complex life cycle which include hypnozoites that may cause relapse, renders the Plasmodium vivax vaccine development quite challenging. The present study explored the publication trends in Plasmodium vivax vaccine research over 25 years (2001-2025) using a PubMed-based bibliometric approach. A total of 339 publications were analyzed using the Bibliometrix package in R. The analysis examined publication patterns, journal contributions, author productivity, countrywise research output, vaccine candidates and major research themes. This analysis illustrates how the scope of Plasmodium vivax vaccine research has grown and highlights contribution of different countries, researchers and journals towards the development of this field. It also underlines how the research priorities have shifted focus among different vaccine candidates and an understanding of the stages of parasites life cycle. Over the past 25 years, research in Plasmodium vivax vaccine development predominantly focused on immunology, genetics, and molecular characterization As we review the publication trends for the past 25 years, we get a better understanding of the progress in this field, we can simply identify the areas which received considerable attention and also the sectors which demand further research. The input may help to address some of the challenges associated with the development of an effective vaccine for Plasmodium vivax and the direction of future studies.

Keywords: Plasmodium vivax; malaria vaccine; bibliometric analysis; vaccine candidates; genetic diversity; thematic evolution.

1. Introduction

Plasmodium vivax, is widespread human malaria parasite is still a public health problem, especially in South and Southeast Asia, the Western Pacific, and parts of Central and South America. P. falciparum has received attention over the years, while P. vivax adds a large share to the global malaria burden. It also brings its own challenges for control and elimination (Mendis et al., 2001). This parasite can form dormant liver-stage hypnozoites, which can reactivate months or even years after the infection, leading to malaria coming back again and again, making its elimination difficult. A vaccine against P. vivax is a research goal. It could stop disease, reduce transmission, and help eliminate malaria. Scientists have looked at candidate antigens. These include circumsporozoite protein (PvCSP), thrombospondin-related protein (PvTRAP), Duffy-binding protein (PvDBP), merozoite surface protein 1 (PvMSP1), apical membrane antigen 1 (PvAMA-1), and transmission-blocking antigens such as Pvs25 and Pvs230. Still, making a vaccine is not easy. The parasite has a complex life cycle, antigens vary a lot, it forms hypnozoites and there no reliable continuous in vitro culture system (Duffy & Gorres, 2020; Veiga et al., 2023; Dickey & Tolia, 2023). Researchers have found possible targets, but so far, no licensed vaccine exists that works only against P. vivax malaria. Genetic diversity is particularly important because variations in vaccine-target antigens may influence immune recognition and the breadth of protection. Siwal (2022) reported geographical variation in circumsporozoite protein (PvCSP) nucleotide and haplotype diversity among Indian P. vivax populations. In addition, Siwal et al. (2026) reviewed major molecular targets and challenges in P. vivax vaccine development. These studies highlight the importance of understanding antigen diversity alongside developments in vaccine research. Bibliometric analysis provide a systematic approach to examining publication trends, influential authors and journals, country contributions, research collaborations, and changes in major research themes. Previous studies have analysed global malaria vaccine research (Garg et al., 2009; Chutiyami, 2024), while De Couvreur et al. (2023) examined publication patterns and thematic developments in parasite vaccine research more broadly. However, a focused assessment of P. vivax vaccine research over an extended period is needed to understand the evolution of research priorities, the distribution of attention across candidate antigens, and emerging areas of investigation. Considering the continuing public health importance of P. vivax, the absence of an approved vaccine, and the challenges associated with vaccine development, the present study conducted a bibliometric

analysis of PubMed-indexed publications from 2001 to 2025. The study aimed to identify prominent research areas, changing research priorities, and potential gaps in P. vivax vaccine research.

2. Materials and Methods

A search of PubMed was conducted in October 2026 to identify publications related to Plasmodium vivax vaccine research published between 2001 and 2025. The retrieved records were exported from PubMed and analysed using Biblioshiny, the web-based interface of the Bibliometrix package in RStudio. The search strategy combined Plasmodium vivax terms in the Title/Abstract field with vaccine-related terms in the Title/Abstract field and was restricted to publications dated 1 January 2001 to 31 December 2025.

2.1 Complete Pubmed Search String

("Plasmodium vivax"[Title/Abstract] OR "P. vivax"[Title/Abstract]) AND (vaccine[Title/Abstract] OR immunization[Title/Abstract] OR immunisation[Title/Abstract] OR vaccination[Title/Abstract]) AND ("2001/01/01"[Date - Publication] : "2025/12/31"[Date - Publication]).

The initial dataset contained 802 records. Screening based on titles and candidate-antigen relevance identified 341 potentially eligible publications. Following a subsequent quality check, two records were excluded, leaving 339 unique publications for the final analysis. The dataset included PubMed identifiers (PMIDs), publication years, titles, candidate-antigen information, vaccine-stage classifications, and screening and quality-decision fields. Publications without recorded candidate-antigen or vaccine-stage information were treated as unclassified for the respective variables. Candidate-antigen and vaccine-stage categories were allowed to overlap when a publication addressed multiple targets or developmental stages. Bibliometric analysis was performed in R using the Bibliometrix workflow (Aria & Cuccurullo, 2017). Descriptive indicators were used to summarize annual publication output, author productivity, journal contributions, corresponding-author countries, and country representation based on institutional affiliations. Frequencies of vaccine candidates and developmental stages were also examined. Author and country collaboration networks were analysed to describe patterns of research collaboration. MeSH terms and keywords were examined through co-occurrence analysis, thematic mapping, and thematic evolution. Thematic evolution was assessed across three periods: 2001–2010, 2011–2017, and 2018–2025. Network and thematic results were interpreted descriptively. Citation impact was not assessed because verified citation counts were unavailable in the retrieved PubMed/MEDLINE metadata. Zero values generated by the workflow were therefore not interpreted as confirmed zero-citation counts, and citation rankings and citation-impact indicators were excluded.

3. Results

A total of 339 PubMed-indexed publications on Plasmodium vivax vaccine research published between 2001 and 2025 were included in the analysis. These publications appeared in 88 journals and involved 1,447 authors, with 2,751 author appearances. The average number of authors per publication was 8.12, and five publications were single-authored. International co-authorship accounted for 30.09% of publications. The annual publication growth rate was 4.06%, while the mean document age was 11.4 years (Table 1).

Table 1. Overall bibliometric characteristics of P. vivax vaccine research, 2001–2025

Indicator	Result
Publications	339
Journals/sources	88
Authors	1,447
Author appearances	2,751
Single-authored publications	5
Mean authors per publication	8.12
International co-authorship	30.09%
Annual growth rate	4.06%
Mean document age	11.4 years

Publication output varied over the study period. The highest number of publications was recorded in 2011 (29), followed by 2017 (22) and 2024 (21). Nineteen publications appeared in 2016, while 2013 and 2022 each recorded 18 publications. Thirteen publications were recorded for 2025. Soares IS was the most productive author, with 33 publications, followed by Sattabongkot J (32), Herrera S (28), Arevalo-Herrera M (27), and Tsuboi T (26). Among journals, Vaccine published the highest number of papers (51), followed by Malaria Journal (25). PLOS Neglected Tropical Diseases and the American Journal of Tropical Medicine and Hygiene each published 18 papers, while Infection and Immunity published 17. Based on corresponding-author affiliation, the United States contributed the largest number of publications (57), followed by Brazil (41), Colombia (35), and India (31). Japan contributed 19 publications, Korea 17, and China and Thailand 16 each. Analysis of institutional affiliations also identified Brazil, the United States, China, Colombia, India, and Thailand among the frequently represented countries. These counts may overlap because individual publications can involve researchers from multiple countries.

The collaboration network among the 30 leading authors contained 488 edges and had a modularity of 0.5895, suggesting the existence of collaborative groups. The country collaboration network comprised 20 countries and 313 edges, with a modularity of approximately 0.126.

PvDBP was the most frequently reported vaccine candidate, appearing in 48 publications. PvCSP and Pvs25 each appeared in 47 publications, followed by PvMSP in 46 and PvAMA-1 in 41. Pvs28 appeared in 15 publications. Pvs230 was also identified, whereas PvRBP and PvTRAP each appeared in seven publications. PvCelTOS was reported in six publications. The vaccine candidate categories were not mutually exclusive, as a single publication could address more than one antigen. With respect to vaccine stages, 124 publications concerned blood-stage vaccines, 48 focused on pre-erythrocytic vaccines, and 41 addressed transmission-blocking vaccines. Eight publications addressed both pre-erythrocytic and transmission-blocking approaches, while three covered other or multiple stages. The vaccine stage was not specified in 115 publications (Table 2).

Table 2. Leading vaccine candidates and distribution by vaccine stage

Category	Publications (n)
Vaccine candidates	
PvDBP	48
PvCSP	47
Pvs25	47
Pvs28	15
Pvs230	Not reported
PvMSP	46
PvAMA-1	41
PvTRAP	7
PvRBP	7
PvCelTOS	6
Vaccine development stages	
Blood-stage	124
Pre-erythrocytic	48
Transmission-blocking	41
Pre-erythrocytic + transmission-blocking	8
Other/multiple stages	3
Unspecified stage	115

Note: Vaccine candidate categories may overlap because a publication can investigate more than one candidate. Pvs230 was identified in the Results, but its publication count was not available in the tabulated dataset. Vaccine-stage categories are reported as provided in the dataset.

The MeSH and keyword analysis indicated that P. vivax immunology, malaria vaccines, genetics, antibodies, antigens, molecular sequence data and genetic variation were key research areas. The keyword co-occurrence network had a modularity of 0.1172, underscoring links among immunology, vaccine research, antigenic targets and molecular genetics. In the thematic map (Figure 1), P. vivax immunology and molecular sequence data were identified as major themes. Genetics and immunology were located near the centre of the map. Escherichia coli genetics and metabolism constituted a specialised theme. Malaria vivax prevention and control and blotting/western appeared in the section of the map representing emerging or declining themes.

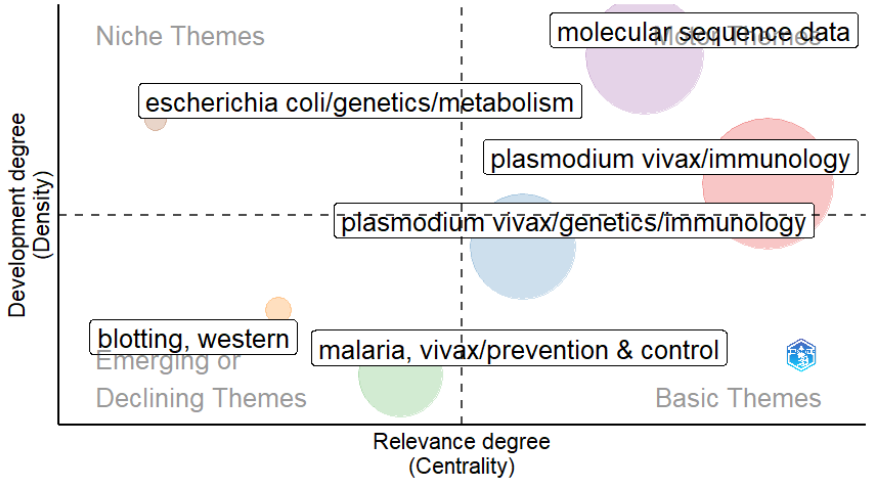

Figure 1. Thematic map of P. vivax vaccine research based on keyword/MeSH co-occurrence. Themes are positioned according to centrality (relevance) and density (development).

The thematic evolution over three periods—2001–2010, 2011–2017 and 2018–2025—revealed changes in research focus (Figure 2). From 2001 to 2010, immunology, antibodies, genetics and molecular sequence data were the main themes. Between 2011 and 2017, vaccine-, antigen-, protein- and immunology-related topics were prominent. Between 2018 and 2025, immunology, genetics, and molecular sequence analysis continued to play important roles, indicating that research remained focused on immune responses and parasite variation.

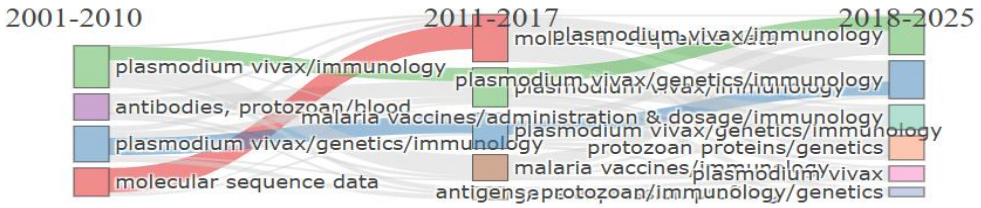

Figure 2. Thematic evolution of P. vivax vaccine research across three periods: 2001–2010, 2011–2017, and 2018–2025 Citation impact was not assessed because verified citation counts were unavailable in the retrieved PubMed/MEDLINE metadata. Therefore, zero values generated by the workflow were not interpreted as genuine zero-citation counts, and citation rankings were excluded.

4. Discussion

This study examined publication trends and research themes in Plasmodium vivax vaccine research from 2001 to 2025. The analysis of 339 publications showed contributions from several countries, continued interest in different vaccine candidates, and a strong focus on immunology, genetics, and molecular characterization. Previous bibliometric studies have examined global malaria vaccine research (Garg et al., 2009; Chutiyami, 2024), while De Couvreur et al. (2023) studied parasite vaccine research more broadly. The present study adds to these investigations with focus being specifically on P. vivax vaccine research and changes in its major research themes over 25 years. PvDBP, PvCSP, Pvs25, PvMSP, and PvAMA-1 were among the frequently represented vaccine candidates. These antigens are associated with different stages of the parasite's life cycle and reflect the range of approaches being explored for vaccine development. Previous reviews have discussed blood-stage, pre-erythrocytic, and transmission-blocking strategies (Mueller et al., 2015; De et al., 2021; Veiga et al., 2023; White & Chitnis, 2022). Frequent publication of a candidate does not establish its protective efficacy or clinical readiness; it only reflects the research attention it has received. PvCSP remains an important target for pre-erythrocytic vaccine research. Genetic variation in this antigen may affect immune recognition and vaccine-induced protection. Siwal (2022) reported geographical variation in PvCSP nucleotide and haplotype diversity among Indian P. vivax populations, highlighting the need to consider parasite diversity when evaluating vaccine candidates. Siwal et al. (2026) also reviewed the major molecular targets and challenges in P. vivax vaccine development. Blood-stage vaccine research formed the largest classified group in this analysis. PvDBP, PvMSP1, and PvAMA-1 have received considerable attention because of their roles in parasite invasion and related biological processes. However, antigenic polymorphism and differences in immune responses are the challenges in developing vaccines that provide broad protection (Reyes-Sandoval & Bachmann, 2013; De et al., 2021; Kar & Sinha, 2022; Dickey & Tolia, 2023). Transmission-blocking candidates, including Pvs25, Pvs28, and Pvs230, offer another approach by targeting parasite development in mosquitoes (Tachibana et al., 2022; Duffy & Gorres, 2020).

Together, these candidates show the range of strategies being investigated, although publication frequency alone cannot determine which approach is most promising. United States, Brazil, Colombia, and India were among the leading contributors based on corresponding-author affiliation. Collaboration networks also showed connections between researchers from different countries. Earlier bibliometric studies reported major contributions from countries including the United States, United Kingdom, and Australia (Garg et al., 2009; Chutiyami, 2024). Differences may reflect variations in study periods, databases, and research scope. However, publication output does not necessarily correspond to malaria burden or the representation of endemic populations in research. Greater collaboration with researchers from malaria-endemic regions would help address questions related to regional parasite diversity. Thematic analysis identified immunology, genetics, and molecular sequence characterization as major research areas. These topics are closely related to understanding parasite variation and host immune responses during vaccine development. Similar changes in research themes have been discussed by De Couvreur et al. (2023), while other reviews have highlighted the importance of antigen discovery and vaccine design (Duffy & Gorres, 2020; Veiga et al., 2023). Nevertheless, publication trends reflect research interests rather than experimental progress or successful vaccine development. This study has some limitations. First, only PubMed-indexed publications were included, so relevant studies from other databases may have been missed. Second, the classification of vaccine candidates and developmental stages depended on the information available in individual publications, and some records lacked sufficient details. Third, publication counts and collaboration indicators do not directly measure research quality, vaccine efficacy, or clinical impact. Citation impact was also not assessed because verified citation counts were unavailable in the retrieved metadata. Despite these limitations, the analysis provides an overview of P. vivax vaccine research over 25 years, including frequently studied antigens, major contributing countries, collaborations, and research themes. Further studies combining population-level genetic data, immune responses, and experimental evidence may help address existing gaps and support the development of effective vaccines against P. vivax.

5. Conclusion

This bibliometric analysis of 339 publications gives a clear picture of Plasmodium vivax vaccine research from 2001 to 2025. PvDBP, PvCSP and Pvs25 were among the most common vaccine candidates. The main themes that appeared repeatedly were immunology, genetics and molecular sequence characterisation. Many countries contributed to this research, and the collaboration networks show that this field has international participation. Still, the number of publications does not prove that a vaccine is effective or ready for clinical use. Future studies should bring together parasite diversity, immune-response data and approaches targeting different stages of the parasite's life cycle. Looking

at additional bibliographic databases and using verified citation information could provide an even clearer picture of research trends and their impact.

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