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Bibliometric analysis of artemisinin combination therapy efficacy publications on SCOPUS and PUBMED databases

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Abstract

In line with research efforts towards malaria control and eradication, this study was proposed to provide a bibliometric summary of research output on ACT resistance/ therapeutic efficacy.

Keywords related to ACT efficacy were used to retrieve literature using the PUBMED and SCOPUS databases.

In total we obtained 7082 and 3031 journal articles were retrieved from the databases respectively. The number of publications on SCOPUS was within the same range of 310-370 except for 2023 which recorded only 207 publications, while for PUBMED, publications showed a noticeable increase between 2006 and 2015. The malaria journal was well represented in both databases with 195, 2.7% appearance in PUBMED and 588, 19.4% in SCOPUS. Although it was the most productive journal in SCOPUS, in PUBMED we had BMC medicine (333, 4.7%). Publications in SCOPUS recorded an average yearly citation of 13.8, further individual analysis showed that 533, 7.5% of publications were cited eleven to twenty times, followed closely by 525, 7.4% of the publications with six to 10 citations. Analysis of Author contribution showed majority of publications in the authorship of 6 and above.

Keywords: Bibliometric analysis; Artemisinin combination Therapy; Therapeutic failure; Authorship pattern; Citation; Source journal

1. Introduction

Malaria, a tropical disease remains a public health concern, particularly in developing countries with Sub-Saharan Africa leading in malaria prevalence studies [1]. Malaria infection is caused by parasites of *Plasmodium* genus and transmitted by a bite of female anopheles mosquito. In 2021, WHO reported an estimated malaria case of 68 million [1]. The majority of antimalarial medications function by targeting the erythrocytic stage of the parasite and therapeutic agents of choice have revolved over time. Quinine obtained from the bark of the Cinchona (Quinnia) tree [2], which was discontinued due to poor tolerance, and compliance with its dosing. Quinine birthed other derivatives such as quinidine, cinchonine and cinchonidine that are all effective against malaria with cure rates >98% as of the 1860s [3]. Following the reported cases of quinine and chloroquine resistance, Artemisinin combination therapy (ACT) was introduced. ACTs with mechanisms of action ranging from interference with parasite transport proteins, disruption of parasite mitochondrial function, modulation of host immune function and inhibition of angiogenesis [4].

Artemisinin resistance characterized by slow parasite clearance [5,6,7] has become a great threat to the achievements recorded in malaria chemotherapy using ACTs. With reports of ACT resistance from parts of Asia and East Africa, there

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is a need to evaluate the scientific productions with regards to ACT from inception till date. Therefore, the analysis was aimed at providing a bibliometric summary of publications on ACT resistance/therapeutic efficacy. The study would be looking at all publications published on ACT resistance/ therapeutic efficacy and available in PUBMED or SCOPUS databases, discussing the following aspects: publication outputs, source journals, citations, authorship, etc.

2. Methods

2.1. Data source

Data for this analysis were retrieved from SCOPUS and PUBMED databases on October 2023 and December, 2023 respectively. Articles published on Artemisinin efficacy were searched on both data bases. The following keywords: (Artemisinin OR Dihydroartemisinin OR Artemether OR Artesunate OR ACT) AND (Clinical-trial OR randomized OR trial) AND (Malaria OR Falciparum OR Ovale OR Vivax OR Malariae) were used in the study and chosen based on already published literatures. In addition, the search had no time limit, other filters used were; language set at only articles published in English language and human clinical trials.

2.2. Bibliometric analysis

Data extracted from the databases were saved as CSV files before being converted to Excel documents for further analysis using Excel version 2021. Bibliometric indicators such as the number of publications by year and for authors, citations, author network, and source journal were extracted. In the process of the analysis, all irrelevant information was removed, same was done for data that were duplicates were applicable.

3. Results

The study is a bibliometric analysis based mainly on the scholarly information of authors who have published articles in PUBMED and SCOPUS on the efficacy of artemisinin-based medications. The study is targeted at studying bibliographic features of articles and citation analysis of references. Information from each database was analyzed individually using the Excel workbook. A total of 7082 and 3031 articles were retrieved from PUBMED and SCOPUS respectively that were in line with the search terms.

3.1. Analysis of yearly distribution of Publications

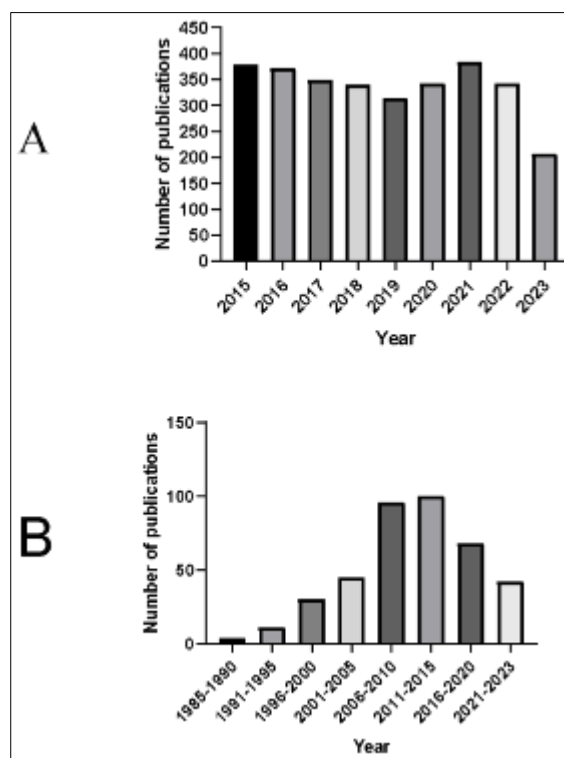


Figure 1 Yearly population growth in (A) SCOPUS, (B) PubMed

Figure 1 and 2 shows the graphical trends in the number of publications within the study scope published in varied years for SCOPUS and PUBMED databases respectively. For SCOPUS, a total of 9 unique years ranging from 2015-2023, with of 3031 published articles were obtained. While for PUBMED our search recorded 38 years, with a total of 7082 published articles. The highest number of 23 publications in PUBMED was recorded in the year 2020, with a rate of 6.0%, while 1988, 1991 and 1994 all had just one article published in the subject area of interest. The other publications in SCOPUS on the subject area, ranging from 207 to 384, per year with 2021 recording the highest (Tables 1 and 2)

3.2. Analysis on authors' contribution/patterns

Single authorship (SA) or multiple authorship (MA), was analyzed to determine their percentage contribution as well as study their degree of collaboration. Figure 3 describes the latter for SCOPUS, with the majority of authors publishing their research findings in groups of 6 to 10, this is followed closely by groups of 1 to 5 authors. This is in line with our analysis in Table 1 showing a higher number of multiple authorship (2980, 98.83%), with the degree of collaboration at 0.98 ± 0.01 , whereas only 49 articles published between 2015 and 2023 had a single authorship, with 2015 and 2016 having 9 and 8 SA published articles respectively.

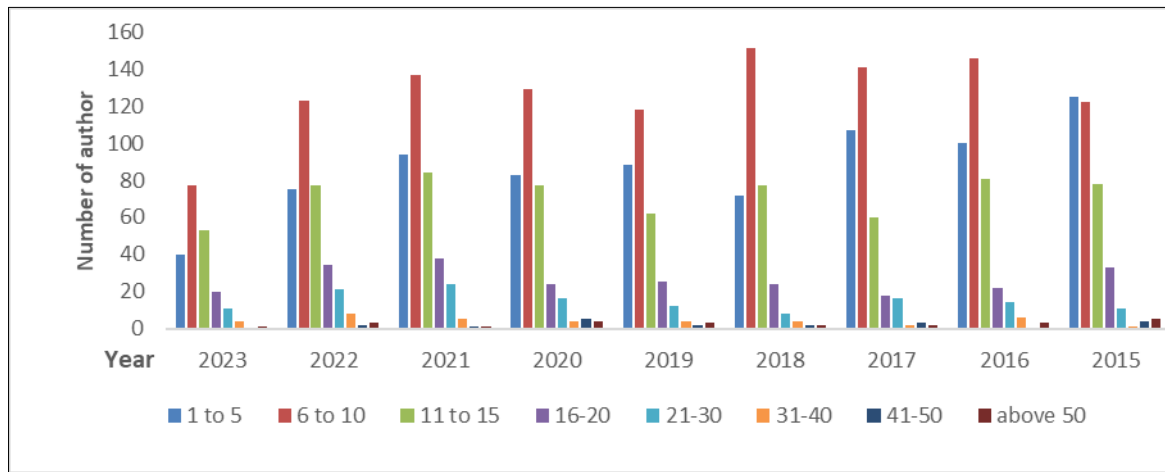


Figure 2 SCOPUS author citation index

Table 1 Number of authors and degree of collaboration

SCOPUS database					PUBMED database				
Year	SA	MA	SA+MA	Degree of Collaboration	Year	SA	MA	SA+MA	Degree of Collaboration
2023	4	202	206	0.980582524	1985 - 1990	1	3	4	0.75
2022	4	339	343	0.988338192	1991 -1995	0	11	11	1
2021	4	380	384	0.989583333	1996 - 2000	0	30	30	1
2020	6	336	342	0.98245614	2001 - 2005	0	45	45	1
2019	4	310	314	0.987261146	2006 -2010	0	96	96	1
2018	5	335	340	0.985294118	2011 - 2015	1	99	100	0.99
2017	5	344	349	0.985673352	2016 - 2020	1	67	68	0.985294
2016	8	364	372	0.978494624	2021-2023	0	42	42	1
2015	9	370	379	0.976253298	Total	3	393	396	7.725294
Total	49	2980	3029	0.983823044					

For articles published in the PUBMED database (Table 2), the study recorded a total of 393 multiple authored articles and 3 single authored articles, from 1985 to 2023. The SA occurred in 1985, 2011 and 2018, while the grouped year with the highest number of MA was 2011-2015 with 99 articles, followed closely by 2006-2010 with 96 articles and 2016-202 with 67 articles. To determine the degree of collaboration quantitatively, the formula used by Kannan & Thanuskodi [11] was used. Degree of collaboration (C) = MA/MA+SA, in the present study, the value of C is 0.992 and 0.984 for PUBMED and SCOPUS articles on the subject respectively, thus showing a high joint author contribution in both databases.

3.3. Citation analysis

3.3.1. Number of citations per publication year

Author information, yearly or article citation was carried out on SCOPUS journals only, as information obtained from PUBMED was lacking on the above sub-heading as at the time of data collection.

Table 2 Year-wise distribution of citation

Year	Citation	No of papers	Average No of citation /paper	Cumulative	
				Citation	Percentage
2015	10189	379	26.88390501	10189	23.04005
2016	8930	372	24.00537634	8930	20.19311
2017	7277	349	20.85100287	7277	16.45524
2018	6245	340	18.36764706	6245	14.12161
2019	4289	314	13.65923567	4289	9.698573
2020	3817	342	11.16081871	3817	8.631255
2021	2576	384	6.708333333	2576	5.825023
2022	818	343	2.38483965	818	1.849716
2023	82	207	0.396135266	82	0.185424
Total	44223	3030	124.4172939	44223	100

Table 2 shows the distribution of citation by year of article publication. Over the 9 years (2015-2023), 3030 articles with a total of 44,223 citations were recorded. Total average citation to article was 124.42, with the number of citations to article varying across the different publication years. Study data, revealed that articles published in 2015 had the highest number of citations at 10,189 with average number of citations per paper at 26.88.

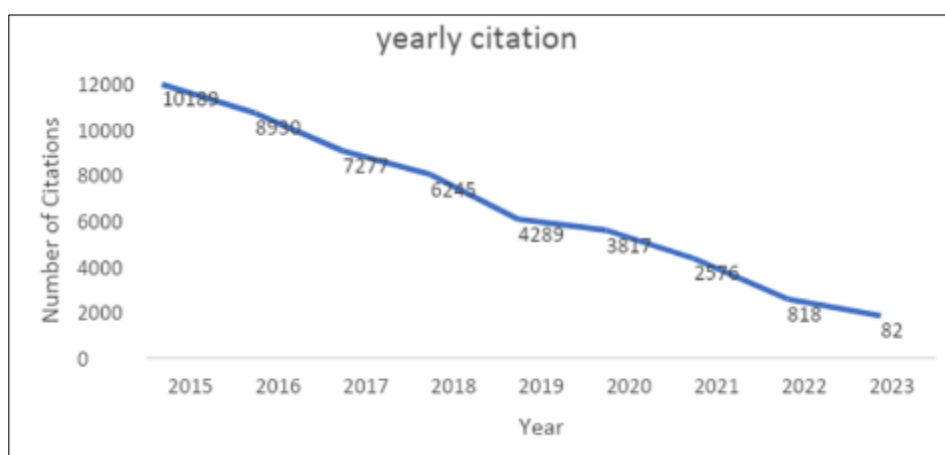


Figure 3 Yearly citation index of SCOPUS publications

Following 2015 closely were articles published in 2016 with 8,930 and 24.00 cumulative citations and average no of citation per paper respectively. The study also showed a decrease in the citation index with each year as shown in Figure 4, this is not entirely a negative outcome as it could potentially mean that authors reference primary sources of their research information.

3.3.2. Author and article citation

To determine the contribution of different first authors obtained in the course of data collection, the analysis sorted out all first authors and determined the number of publications they appeared in. following this, of the 3031 publications, we had a total of 2484 non-duplicate first authors. the data in Figure 5 describes the number of authors that had between 1 and 7 publications in the data set, with 7 being the highest we got in the course of our analysis. Only one author in the person of Sowunmi A, had up to 7 publications in the bunch, with 66, 281, and 2100 having 3,2 and 1 publications respectively. From PUBMED database, Sowunmi also recorded the highest number of publications with 13 articles, followed closely by Karbwang J with 8 articles and Valecha N, Looareesunwan S, and Na-Bangchange K, with 8 articles each.

Of the 3031 publications obtained from SCOPUS, 553 and 525 had the highest citations, falling between 11-20 and 6-10, respectively. Few publications, 1.42% made the 101 and above citation range, with 13 having a citation index of above 200.

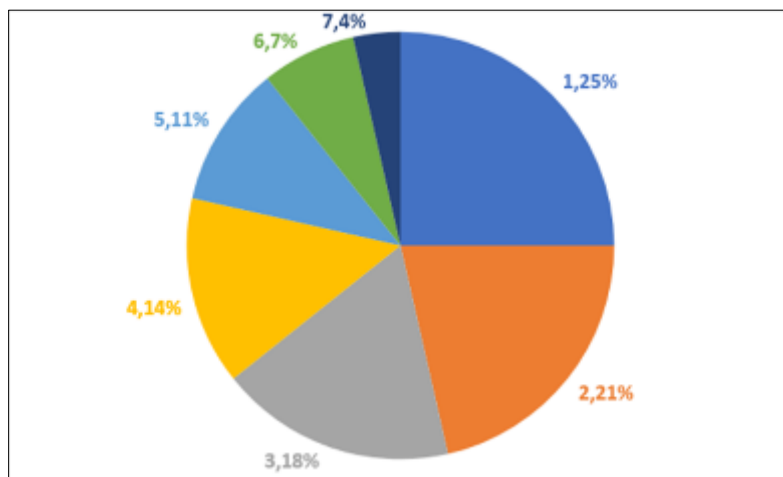


Figure 4 First Author publications

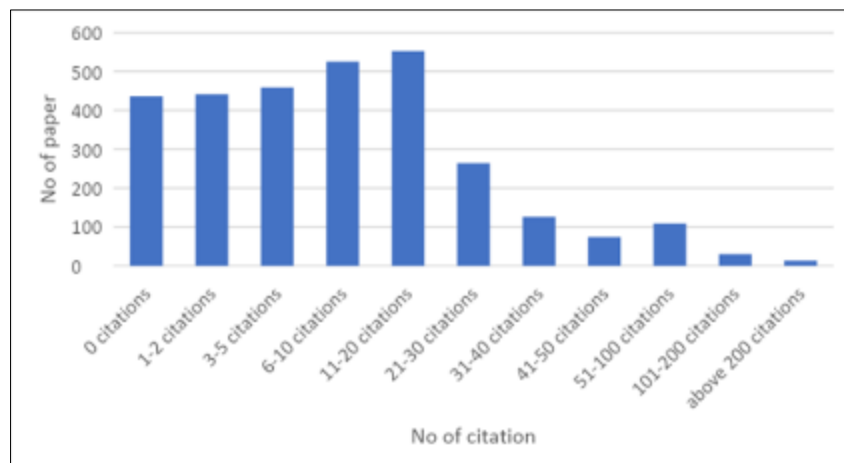


Figure 5 First author citation index

We also went further to determine the first twenty articles with the highest citation index and this is outlined in Figure 5, with full details of each paper, showing their title, source journal, publication year, citation and first author in Table

4. Of the 20 articles, eight were published in 2015, five in 2017, four in 2016, while 2017, 2020 and 2021 each recorded on one publication. 30% of the 20 articles with the highest citation index were published with The Lancet Infectious Diseases, followed closely by Nature journals with 20% while New England Journal of Medicine and PLoS journals had only 2% presence in the list.

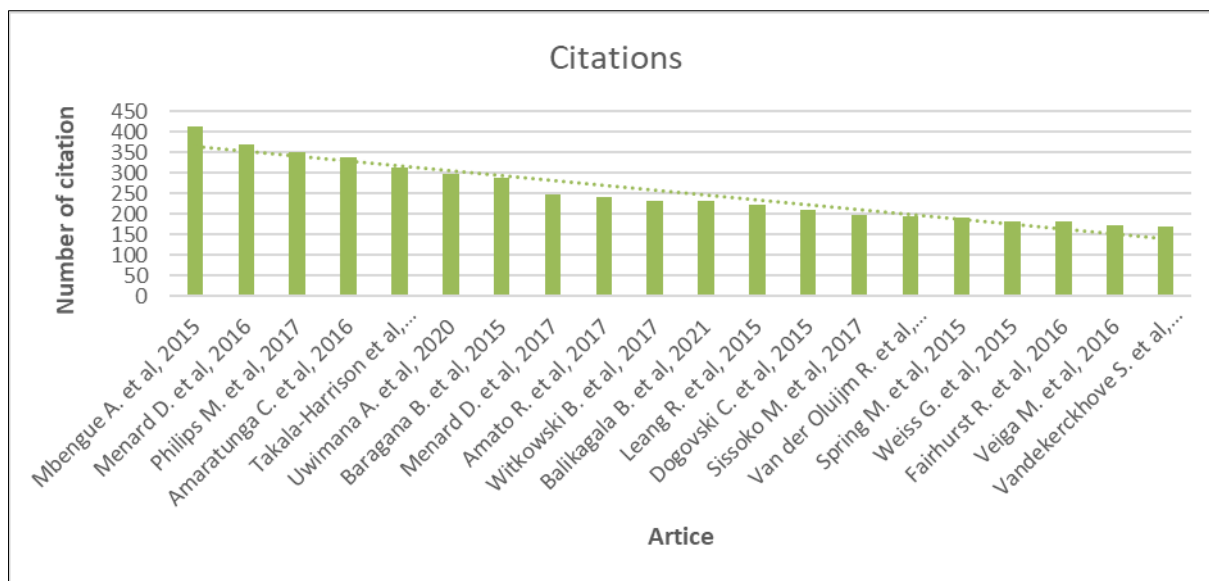


Figure 6 Articles with the strongest citation

Table 3 High-frequent citation articles

Rank	Title	Journal	Year	Citation	Reference
1	“A molecular mechanism of artemisinin resistance in Plasmodium falciparum malaria”	Nature	2015	412	Mbengue A. et al, 2015
2	“A worldwide map of Plasmodium falciparum K13-propeller polymorphisms”	New England Journal of Medicine	2016	371	Menard D. et al, 2016
3	“Malaria”	Nature Reviews Disease Primers	2017	351	Philips M. et al, 2017
4	“Dihydroartemisinin-piperaquine resistance in Plasmodium falciparum malaria in Cambodia: A multisite prospective cohort study”	The Lancet Infectious Diseases	2016	340	Amaratunga C. et al, 2016
5	“Independent emergence of artemisinin resistance mutations among Plasmodium falciparum in Southeast Asia”	Journal of Infectious Diseases	2015	313	Takala-Harrison et al, 2015
6	“Emergence and clonal expansion of in vitro artemisinin-resistant Plasmodium falciparum kelch13 R561H mutant parasites in Rwanda”	Nature Medicine	2020	298	Uwimana A. et al, 2020
7	“A novel multiple-stage antimalarial agent that inhibits protein synthesis”	Nature	2015	288	Baragana B. et al, 2015

8	“Antimalarial drug resistance: a threat to malaria elimination”	Cold Spring Harbor Perspectives in Medicine	2017	249	Menard D. et al, 2017
9	“Genetic markers associated with dihydroartemisinin-piperaquine failure in Plasmodium falciparum malaria in Cambodia: a genotype-phenotype association study”	The Lancet Infectious Diseases	2017	243	Amato R. et al, 2017
10	“A surrogate marker of piperaquine-resistant Plasmodium falciparum malaria: a phenotype-genotype association study”	The Lancet Infectious Diseases	2017	233	Witkowski B. et al, 2017
11	“Evidence of artemisinin-resistant malaria in Africa”	New England Journal of Medicine	2021	231	Balikagala B. et al, 2021
12	“Evidence of plasmodium falciparum malaria multidrug resistance to artemisinin and piperaquine in Western Cambodia: Dihydroartemisinin-piperaquine open-label multicenter clinical assessment”	Antimicrobial Agents and Chemotherapy	2015	222	Leang R. et al, 2015
13	“Targeting the Cell Stress Response of Plasmodium falciparum to Overcome Artemisinin Resistance”	PLoS Biology	2015	212	Dogovski C. et al, 2015
14	“Safety and efficacy of PfSPZ Vaccine against Plasmodium falciparum via direct venous inoculation in healthy malaria-exposed adults in Mali: a randomised, double-blind phase 1 trial”	The Lancet Infectious Diseases	2017	197	Sissoko M. et al, 2017
15	“Determinants of dihydroartemisinin-piperaquine treatment failure in Plasmodium falciparum malaria in Cambodia, Thailand, and Vietnam: a prospective clinical, pharmacological, and genetic study”	The Lancet Infectious Diseases	2019	196	Van der Oluim R. et al, 2019
16	“Dihydroartemisinin-piperaquine failure associated with a triple mutant including kelch13 C580Y in Cambodia: An observational cohort study”	The Lancet Infectious Diseases	2015	191	Spring M. et al, 2015
17	“Revealing the Sequence and Resulting Cellular Morphology of Receptor-Ligand Interactions during Plasmodium falciparum Invasion of Erythrocytes”	PLoS Pathogens	2015	183	Weiss G. et al, 2015
18	“Artemisinin-resistant Plasmodium falciparum malaria”	Microbiology Spectrum	2016	181	Fairhurst R. et al, 2016
19	“Globally prevalent PfMDR1 mutations modulate Plasmodium falciparum susceptibility to artemisinin-based combination therapies”	Nature Communications	2016	172	Veiga M. et al, 2016
20	“Quinoline-based antimalarial hybrid compounds”	Bioorganic and Medicinal Chemistry	2015	170	Vandekerckhove S. et al, 2015

3.4. Source journal

Number of publications on ACTs had a fluctuating up and down growth pattern. From PUBMED database, a total of 1564 journals out of the 1874 journals that appeared in the data extracted, had 1 to 5 publications in the bunch. While for SCOPUS database, the study recorded 579 (87.45%) of source journals appearing between 1 to 5 times. Both databases had 1 (0.053%) of source journal appearing 300 times or more. Table 4 shows the first 20 journals used for publication of research articles in line with our study interest as at the time of data collection. This showed that with SCOPUS, Malaria journal, Journal of Antimicrobial agents and chemotherapy and American Journal of Tropical Medicine and Hygiene having the highest appearances while from the PUBMED database, data showed BMC Medicine, Expert Review Anti-Infective Therapy, Malaria Journal, intensive Care Medicine, Journal of Vector Borne Diseases all having 100 appearances. While Malaria Journal with a total of 588 appearances in SCOPUS, inn PUBMED it only recorded 195 appearances below BMC Medicine that had 333 appearances.

Table 4 First twenty journals with highest publications

S/ N	PUBBMED Database		SCOPUS Database	
	Journal name	Publica tion	Journal name	Publica tion
1	BMC Medicine	333	Malaria Journal	588
2	Expert Review of Anti-infective Therapy	203	Antimicrobial agents and chemotherapy	173
3	Antimicrobial Agents and Chemotherapy	198	American Journal of Tropical Medicine and Hygiene	131
4	Malaria Journal	195	PLoS ONE	95
5	Intensive Care Medicine	182	Clinical Infectious Diseases	77
6	Journal of Vector Borne Diseases	102	Journal of Infectious Diseases	62
7	The Journal of Infectious Diseases	85	The Lancet Infectious Diseases	44
8	Clinical Infectious Diseases	73	Scientific Reports	40
9	Parasite Journal	62	BMC Medicine	39
10	European Journal of Clinical Pharmacology	50	BMC Infectious Diseases	35
11	Lancet Global Health	50	International Journal for Parasitology: Drugs and Drug Resistance	31
12	Scientific Reports	49	Nature Communications	29
13	Transactions of the Royal Society of Tropical Medicine and Hygiene	48	Journal of Medicinal Chemistry	27
14	Journal of Dermatological Treatment	46	Acta Tropica	24
15	PLoS One	44	PLoS Medicine	23
16	BMC Infectious Diseases	43	Parasites and Vectors	21
17	Chinese Journal of Integrative Medicine	42	ACS Infectious Diseases	21
18	The Pan African Medical Journal	38	Frontiers in Cellular and Infection Microbiology	21
19	The Lancet Infectious Diseases	38	European Journal of Medicinal Chemistry	21
20	The Journal of Clinical Pharmacology	36	Journal of Antimicrobial Chemotherapy	20

Limitations

The study covered only two scientific databases, PUBMED and SCOPUS, and did not consider articles published in languages other than English, irrespective of their relevance to the subject area.

4. Discussion

This study was aimed at providing an overview of bibliometric summary of publications Artemisinin Combination Therapy (ACT) efficacy. Currently, ACTs are the main stake in malaria chemotherapy [8]. Artemisinin, has been approved and recommended as first-line treatment for uncomplicated falciparum infection. Emergence of antimalarial resistance poses a significant threat, on the targeted control and elimination of the infection, there is the need for early detection of resistance. Over the years, there has been a lot of research on the efficacy and/or resistance of the leading drug in the fight against malaria, the ACTs. This supports the view of WHO on the need to closely monitor this class of drug as a way of curbing future development of resistance.

The journal BMC Medicine and Malaria Journal for PUBMED and SCOPUS respectively were the most cited publications. Malaria Journal also pulled weight in PUBMED publication for ACT efficacy, being the fourth highest cited. Among the first 10 productive journal in both databases, only BMC Medicine had a citation score of above 500. Following Malaria Journal was Antimicrobial agents and chemotherapy, American Journal of Tropical Medicine and American Journal of Tropical Medicine for SCOPUS all with citation above 100 not up to 200, while for PUBMED database, we had Expert Review of Anti-infective Therapy, Antimicrobial Agents and Chemotherapy and Malaria with 203, 198 and 195 citations respectively. Study by Wanida 2022, also puts Malaria Journal as the journal with the most frequently published journal for malaria research.

In 2009, resistance to artemisinin-based medications was first reported in Western Cambodia. Following this, there was a sharp increase in publications from 2010. The rise in the number of publications for ACT efficacy from 2010 till date could be targeted at monitoring the efficacy of the drug as a way combating drug resistance. Citing primary sources is important and ethically necessary too and this is evidently practiced as seen in the set of publication analyzed in the course of this study. Publications in 2015, had the highest average number of citations per paper indicating a possible primary source citation. In addition, SCOPUS publications between 2015 and 2020 pulled a total cumulative citation of 40747 (92.1%).

With increasing multifaceted complex research globally, researchers are seen working in teams and clusters to achieve a significant research outcome. Although this approach is known to be of benefit in the area of research output, concerns about scientific integrity, fair play [9] have been raised as possible challenges with multiple authorship. Co-authorship pattern as a tool can also be used to show type and nature of research collaborations [10]. The present study showed a 98.3% degree of collaboration with 2980 out of the 3031 publications having multiple authors.

5. Conclusion

This paper conducted a bibliometric analysis on artemisinin efficacy from articles published in SCOPUS and PUBMED. The citation and the number of publications between 2015 and 2020 was nearly at the same rank, but by 2022 and 2023 the study a much more decrease of publication. One can say that the number of publications by 2015 up to 2019 could be as a result of rush to study ACTs for possible drug therapy problems following continuous use and abuse for over ten years.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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