African Journal of Pharmaceutical Research & Development
Available online at https://ajopred.com
Vol. 15 No.2; pp. 9-16 (2023)

MALARIA AND ARTEMISININ RESISTANCE: A BIBLIOMETRIC ANALYSIS

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ABSTRACT

With roughly 50 % of the global population at risk for infection, malaria is one of the most serious public health problems in the world. This infection is caused by single-celled protozoa of the genus *Plasmodium*. By the turn of the century, the majority of antimalarial drugs were no longer effective against *Plasmodium falciparum.* However, one year after World Health Organization's final endorsement for the global use of ACTs, an appearance of artemisinin-resistant *Plasmodium falciparum* was seen in the border regions of Thailand and Cambodia and has since spread to other areas on the globe in subsequent years. The purpose of this work is to summarize the knowledge structure and trend of malaria and artemisinin resistance from 2012 to 2022. The VOS viewer application was used to bibliometrically analyze publications from 2012 to 2022. A total of 169 papers that discussed the keywords were used. VOS viewer application was used to produce maps based on the scientific data between the top authors and top terms in clusters. The research trend of artemisinin resistance and malaria was reported to be on the decline from 2019 to 2022. The bibliographic analysis offered an intellectual framework for the study area by identification of research groups and themes. The years with the most publications were 2015-2017, with 23 articles published each year. The most often used keywords in the research were artemisinin resistance (38 occurrences). The spread of artemisinin-resistant *P. falciparum* in significant regions of Southeast Asia threatens to destabilize malaria control globally. One of the most pressing global health concerns today is preventing artemisinin resistance from spreading to Africa, where the consequences for childhood mortality might be severe.

ARTICLE INFO

Received 01 June, 2023
Revised 10 July, 2023
Accepted 13 July, 2023

KEYWORDS

Artemisinin,
Re-emergence,
Sensitivity,
Chemotherapy,
Malaria

INTRODUCTION

With about 50 % of the global population at risk of malarial infection, it is considered one of front-line global health challenge. Malaria is found in 91 nations, mostly in the world's tropical and subtropical climates. However, with globalization, its incidence has practically touched all countries and cases have kept on increasing [1]. Using World Health Organization (WHO) data, it was projected in 2021 that Malaria cases totaled 247 million worldwide,

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with 619,000 fatalities, approximately 80% of malaria deaths in the region occurred in children under the age of five [2]. Malaria claims the lives of about 400,000 people each year [3]. It is transmitted by single-celled protozoan of the genus *Plasmodium* which is spread when the female anopheles mosquito engages in blood meal on human and injects the sporozoites into the blood stream.

The main stay in malaria eradication or drastic reduction in malaria prevalence involves a combination of measure like: vaccination, vector control, chemotherapy with antimalarial drugs, and chemoprophylaxis [1,4]. By the turn of the 20th century, *Plasmodium falciparum* had evolved resistance to the majority of antimalarial drugs then used in Southeast Asia, including chloroquine (CQ), antifolates, and mefloquine (MQ) [5]. With the introduction of artemisinin and its semi-synthetic derivatives, there have been notable landmark achievements in malaria treatment [6-10]. Also, few studies had documented the possibility of treating malaria with some herbal medicines [11-13].

One year after World Health Organization's final endorsement for the global use of ACTs, an appearance of artemisinin-resistant *Plasmodium falciparum* was seen in the border regions of Thailand and Cambodia in 2007-2008 [14]. Also, *Plasmodium falciparum* strains to companion medicines (such as piperaquine) began to emerge and further lowered the efficacy of dihydroartemisinin/piperaquine [15-17]. Just recently in East Africa, artemisinin resistance was reported [18].

The gold standard for detecting resistance *in vivo* continues to be effectiveness studies, such as therapeutic efficacy studies using ACT regimens or specialized clinical studies using artesunate monotherapy alone or after ACT [19].

The purpose of this work is to summarize and investigate the knowledge structure of malaria and artemisinin resistance, as well as to collect a vast number of bibliometric data to demonstrate the present condition of the knowledge network and recent developments in malaria and artemisinin resistance.

METHODOLOGY

Sources of Data

The bibliometric analysis included research journals on malaria, antimalarial activity, and artemisinin resistance published in English between 2012 and 2022 by typology, refereed by pairs, and indexed and available on Google Scholar.

Search Strategy

Specific search terms in English were combined with the title, abstract, and keyword fields. Anti-malarial, sensitivity, re-emergence, chemotherapy, and malaria were stratified, as were the terms that are frequently used to denote them. Articles that were not published in English were cited (n=15), leaving a total of 169 articles in the final analyses. The research framework is shown in Figure 1

Studied Variables

In general, the databases took into account the following variables: kind of scientific articles, co-occurrence of key terms indexed in literature, malaria, antimalarial activity, and artemisinin resistance factors, and were then integrated into a network analysis of research development. Publications were classified and analyzed systematically based on the year of publication, nation, journal, study area, authors, and organizational affiliation.

Data Collection Process

The relational metric indication (keyword co-occurrence) was evaluated and seen using VOS viewer version 1.6.18, and all relevant records retrieved between 2012 and 2022 were categorized using the endnote bibliographic manager. Additional filters were constructed and used to minimize non-specific terms and other topics to refine and improve the database's precision. The visualization of the similarities (VOS) mapping approach was used to determine similarity based on association strength, and a higher number of publications in which two items co-occur shows that the phrases are more closely connected. Words featured in the title or abstract of the articles mentioned here were defined as co-words. Keywords were determined as words that appeared more than 20 times in titles and abstracts from different publications.

RESULTS AND DISCUSSION

Chloroquine, a previously highly successful and cost-efficient antimalarial medication, has lost general potency in the majority of malaria-endemic countries around the world. Artemisinin-based drugs have taken the place of chloroquine. Indiscriminate use of antimalarial drugs has exposed the parasites to the drugs continuously thereby contributing to the emergence of malaria resistance. This indiscriminate use is attributable to self-medication and failure to carry out proper diagnosis of malaria parasite infections before treatment.

Up to 169 papers were retrieved from Google Scholar using the phrases malaria, antimalarial activity, and artemisinin resistance within the study period (2012-2022). The years with the most publications were 2015-2017, with 23 articles published each year. It was also noted that the years 2015 to 2018 had the highest number of articles (52.66% of all papers retrieved), which could imply that the field of study is getting more consolidated. The research trend of artemisinin resistance and malaria together was reported to be on the decline from 2019 with 11 articles, 2020 with 14 articles, 2021 with 7 publications, and 2022 with only one article indexed in Google scholar at the time of research (Figure 2). This might be due to a decline on research relating to malaria resistance following the emergence of the COVID-19 and efforts/researches to its containment.

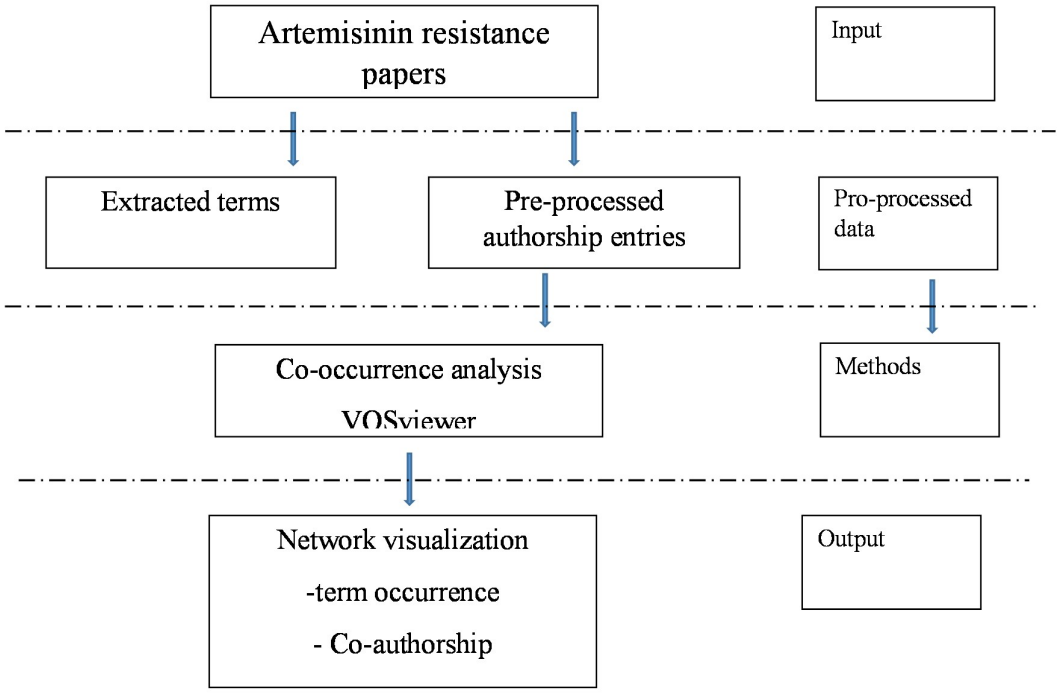

Figure 1: Framework of the study

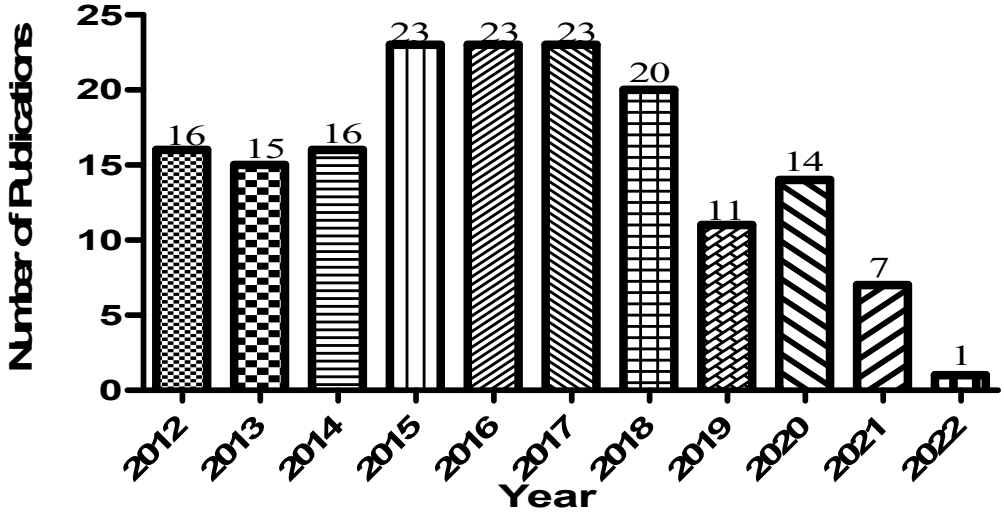

Figure 2: Number of publications by year

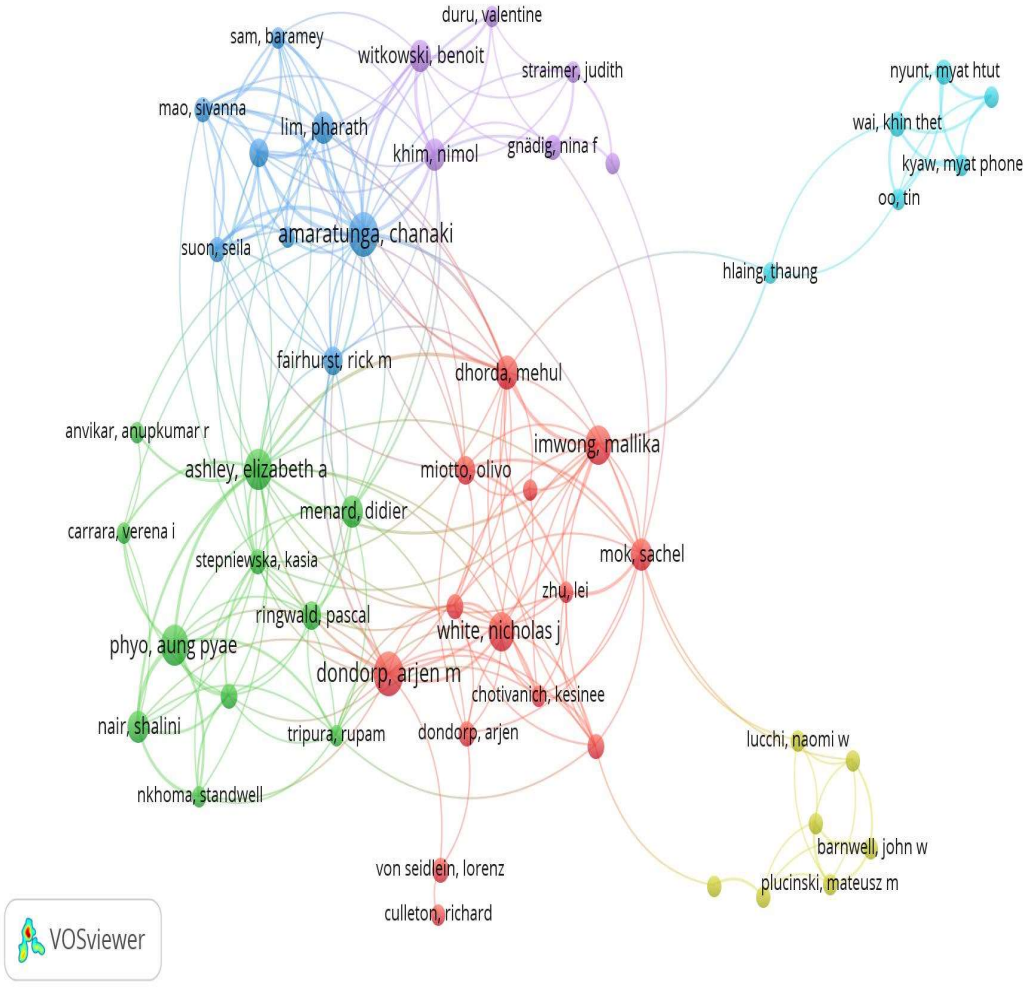

Figure 3: Co-authorship analysis among authors with the publication of articles

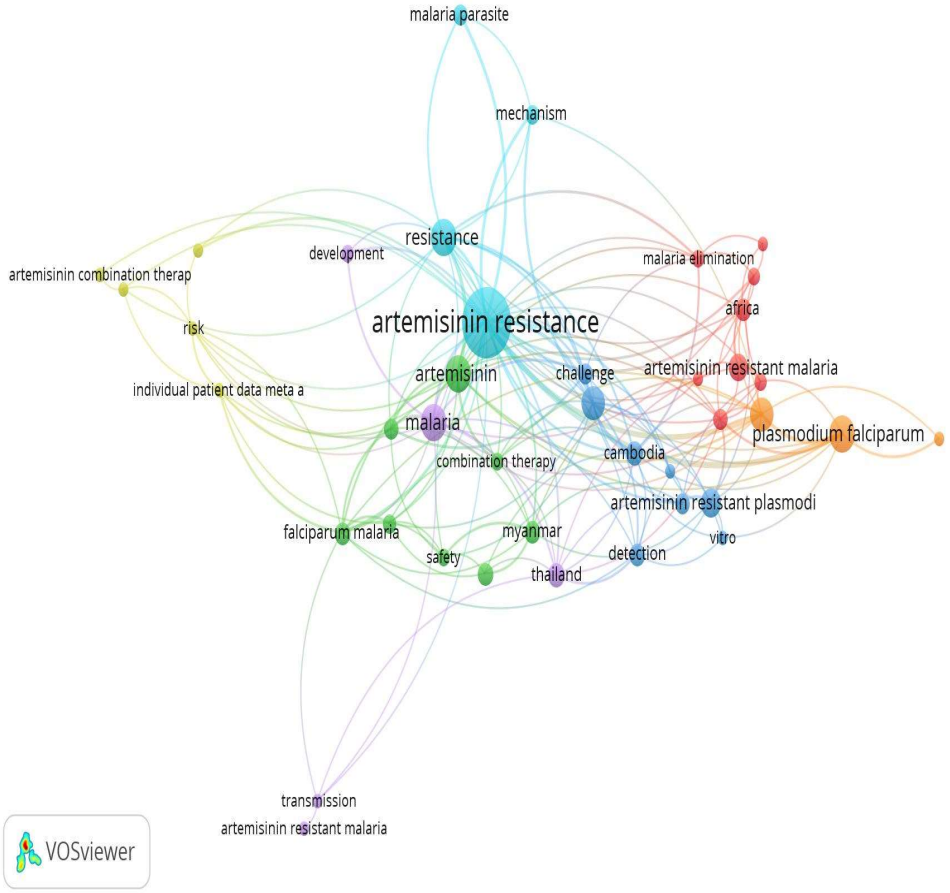

Figure 4: Term occurrence analysis among the various publication of articles

Trends in Research Collaborations

Finding the presence of research groups through co-authorship analysis can help uncover patterns and types of research collaborations in the examined region. Co-authorship analysis revealed seven clusters with a total of 45 items, as shown in Figure 3. Twenty-three (23) of the chosen authors (50%) have only co-authored or published one article. This displays the breadth of prominent research groups in terms of author collaborations. As a result, the items in the clusters were created by co-authors of the same publications. The following clusters stood out among the seven (7) clusters: in the deep blue cluster, Amarantunga Chanaki was the most prominent author in the group and had the most impact on articles linked to the cluster; in the green cluster, Aung Phyo and Ashley Elizabeth were the most prominent authors; in the red cluster, Dondorp Arjen was the most notable author in the group. Apart from malarial research, these authors had featured in other kinds of researches [20, 21, 22, 23] respectively.

Key Research Themes and Trends

Keyword co-occurrence analysis can discover keywords that appear in the same reference, allowing for the identification of commonly used keywords. By finding the frequently used terms, the principal study areas in the research field can be examined. The most often used keywords in the research were artemisinin resistance (38 occurrences), malaria (20 occurrences), resistance (20 occurrences), and *Plasmodium falciparum* (18 occurrences). Figure 4 shows the map of the term co-occurrence among the publications.

Study Limitations

This study focused on literature published only in English Language and for a limited time frame (2012-2022). Additionally, the study utilized only one

database, the Google Scholar. Other more robust data bases like Scopus, Web of Science, EMBASE, Gray literatures and PubMed *et cetera* were not searched and so the study may have missed some vital documents/publications.

CONCLUSION

The spread of artemisinin-resistant *P. falciparum* in significant regions of Southeast Asia threatens to destabilize malaria control globally. One of the most pressing global health concerns today is preventing artemisinin resistance from spreading to Africa, where the consequences for childhood mortality might be severe.

The recent discovery of artemisinin resistance in Africa reinforces the necessity for continuous research into alternatives to artemisinin drugs in the treatment of malaria. More research is required with innovative therapies to contain the increasing pressure of artemisinin resistance.

Funding

Nil.

Declaration of Competing Interest

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

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