Risk of depression and common comorbid mental disorders in persons with malaria: a protocol for a systematic review and meta-analysis

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Protocol

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Abstract

Aim

To estimate the pooled prevalence and incidence of depression and its common comorbid mental disorders in persons with a malarial infection and its neurological complications

Method

We will conduct a systematic review and meta-analysis of studies published between January 1, 1960 and January 1, 2020, reporting the prevalence or incidence of common mental disorders and the risks in people with malaria. We will search the following databases: PubMed (MEDLINE), Scopus, OVID (HEALTH STAR), OVID (MEDLINE) and Joana Briggs Institute EBF Database. No age, geographical location, study-design or language limits will be applied. If multiple languages were used to describe and publish the same data, the English version was selected. This protocol was developed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols guidelines. Three reviewers (MC, YP, YY) will independently screen citations, abstracts and will identify full-text articles for inclusion, extract data and appraise the quality and bias of included studies. Discrepancies will be resolved by consensus or consultation with a fourth researcher (AS). Risk of bias of included studies will be assessed by the Newcastle-Ottawa Quality Assessment Scale. The primary outcomes will be the overall prevalence or incidence of depression and common comorbid mental disorders (CCMDs) in persons with malaria. We will use the random-effects model with a logit transformation of proportions for the pooling of studies. We will assess the between-study heterogeneity using I2 statistics, and Cochrane's Q statistic (significance level < 0.05). We will perform subgroup meta-analyses to investigate geographical differences in mental disorders and risks of different mental disorders. We will conduct a meta-regression analysis, using study level median age, race and gender proportions, the proportion of study population with malaria, and percentage of the study population with a diagnosis of common mental disorders. We will report absolute differences in the overall probability of common mental disorders. The Egger's test and funnel plots will be used to assess publication bias.

Background

Since its discovery in the late 19th century, malaria has imparted a substantial burden of disease upon tropical and subtropical regions throughout the world. While the disease has become preventable and curable with modern practices, developing societies still face many hardships as a result of the disease. According to the latest World malaria report, released by the World Health Organization in December 2019, there were approximately 228 million worldwide cases of malaria in 2018, which lead to 405,000 subsequent deaths that year[1]. Sub-Saharan Africa in particular continues to carry a disproportionate burden of this disease, with the region accounting for 93% of these cases and 94% of deaths in the same 2019 WHO report. While current global efforts continue to develop an effective framework for controlling

malaria infections, these current strategies fail to address the psychological burden that a malarial infection may carry.

Although extensive literature exists to characterize the pathophysiological effects of acute and chronic malarial episodes, much scarcer data exists regarding the psychological factors that may be associated with the manifestation of this disease. In 2017, Jenkins and colleagues were among the first to explore this relationship and found that malaria parasitemia was associated with increased rates of depression and other common comorbid mental disorders (CCMDs) [2]. Of particular importance to this association is the prevalence of cerebral malaria; a severe complication of the disease that occurs in roughly 2% of cases and carries significant risk for neurological impairment. A 2016 cross-sectional study found that cerebral malaria in children was associated with an increased risk for developing long-term mental health disorders [3].

Furthermore, the specific relationship between depression and malaria is complex and currently poorly understood. The debilitating effects of malarial infection may predispose individuals to depression, while depression may likewise predispose individuals to malaria through its impact on immunity and behavior [4]. Despite the paucity of information that exists on this subject, identification of the risk of depression in patients with malaria will inform a more effective approach to its prevention and treatment while adding to a growing understanding of its psychosocial implications.

To our knowledge, there is currently no systematic review and meta-analysis of the pooled incidences of depression in patients with a malarial infection and its neurological complications.

Objectives

The objective of this study is to present a protocol for review and meta-analysis to investigate the prevalence or incidence of depression and its common comorbid mental disorders in persons with malaria.

Specific aims are:

- To examine the global prevalence or incidence of depression and its common comorbid mental disorders (CCMDs) in persons with malaria.
- To delineate the risks of depression and CCMDs in people with malarial neurological complications

Review question

What is the incidence and prevalence of depression and its common comorbid mental disorders in persons with malaria, and what is the odds ratio or hazard ratio of these mental disorders in persons with malaria?

Method

Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols (PRISMA-P) 2015 statement and guidelines will be used to inform the development of this protocol[5,6]. See online supplementary appendix 1 for the checklist.

Patient and public involvement statement

Patients were not involved in the development of this protocol.

Study design

The inclusion criteria consists of studies that:

- Report depression rates in people with malaria, including prevalence, incidence and mortality
- Report rates of depression including its common comorbid mental disorders (CCMDs) in persons with malaria, which includes: anxiety, panic disorder, obsessive-compulsive disorder andpost-traumatic stress disorder [7].
- Were published in any language. If multiple languages were used to describe and publish the same data, the English version was selected.
- Were published between January 1, 1960, to January 1, 2020

The exclusion criteria consists of studies that:

- Were not conducted in humans
- Are case reports and studies that did not report the prevalence or incidence of depression or CCMDs and their OR/HR were excluded
- Are meeting abstracts, review papers, and commentaries

Domain

Studies will be included if they are related to depression or CCMDs and malaria.

Population

Studies will be included that report data generated from participants with malaria, regardless of age, gender and sex.

Outcomes

The primary outcomes of this study will be the overall rates of depression and CCMDs in persons with malaria, as well as the risks of these mental disorders in people with malarial neurologic complications.

Search Strategy

Geographical context

Studies from throughout the world will be included, and regional differences will be estimated through subgroup analysis.

Database searches

The following databases will be searched: PubMed (MEDLINE), Scopus, OVID (HEALTH STAR), OVID (MEDLINE) and Joana Briggs Institute EBF Database. A snowballing method will also be used to search the citation lists of included papers. This will be accomplished by using the 'cited by' tool in Google Scholar. Efforts will be made to contact authors of ongoing studies and in-press literature for information regarding additional studies or supplemental data.

Search Terms

The keyword search will be based on Medical Subject Headings (MeSH) with several combinations of "malaria" OR "cerebral malaria" OR "severe malaria" and "depressive disorder" OR "depression" OR "mental disorder" OR "suicide"

This search strategy will further be adapted and tailored for use with each database, using Boolean operators, truncations, proximity operators and Medical Subject Heading, as appropriate for each database. For a complete list of search terms see online supplementary appendix 2.

Title and abstract screening

Citations will be downloaded into Endnote software, excluding duplicate articles, and will then subsequently be screened by reviewers in two stages. In the first stage, three reviewers will independently assess titles and abstracts for inclusion based on article type and topic. For any articles that are excluded, the reasons for such exclusion will be recorded.

Full-text screening and data extraction

In the second stage of review, full-text versions of selected articles will be retrieved and assessed independently by the three reviewers. Data will be extracted independently from eligible papers during this

final stage of review. In the event of disagreement, the three reviewers will confer and discuss with each other and, if necessary, a fourth review author (AS) to reach consensus. When abstracts and subsequently included papers are not available in English, translators will be sought. The following information will be extracted: first author, country in which the study was conducted, year of publication, study period, research methodology, total sample size, number of patients with depression or depressive symptom, number of patients with other CCMDs, like anxiety, panic disorder and PTSD, number of patients with malaria, percent of study sample that was male, mean age, age with malaria, OR/HR and other findings. In case of missing data, one attempt will be made to contact the corresponding authors of studies by email. If the author fails to provide additional information, a decision will be made as to whether to include the study in the final review.

Assessment of Methodological Quality of the Papers

Three authors will independently assess the quality of the papers included in the review. In anticipation of including observational studies, assessment of methodological quality will be conducted using the Newcastle-Ottawa Quality Assessment Scale, which is a validated tool for assessing quantitative cross-sectional, case-control and cohort studies [8]. Studies will be included regardless of the risk of bias and quality scores, but sensitivity analysis will be conducted to ascertain the impact of their inclusion.

Data synthesis and analysis

The metaprop function of the meta-package in R Statistical Software will be used for analysis [9]. The primary outcomes will be the overall rate of depression and CCMDs and their risks in persons with malaria. A random-effects model will be used with a logit transformation of proportions for the pooling of studies. Confidence intervals will be calculated using the exact binomial (Clopper-Pearson) interval method. If raw proportion cannot be found in the studies, we will calculate the logarithm of OR/RR.

The between-study heterogeneity will be assessed using an I^2 statistic, expressed as percentages of low (25%), moderate (50%), and high (75%). Cochrane's Q statistic will also be used (significance level $p< 0.05$). If it is determined that the between-study heterogeneity is low, a random-effects model still will be applied.

Risk of bias assessment for retained studies

Sensitivity analysis will be performed by use of subgroup meta-analysis to investigate geographical differences in mental disorder risks. Meta-regression analysis will also be conducted using study level median age, and study level gender proportions, year of study, the proportion of study population with malaria, and risk of depression and CCMDs in persons with malaria[10]. Absolute differences will be

reported (per 1000) in the overall probability of depression and CCMDs. The Egger's test and funnel plots will be used to assess publication bias.

Results

Presentation of results and reporting

PRISMA guidelines will be used and the checklist will accompany the publication. Quantitative data will be summarized and presented in tables, forest plots and maps. The prevalence and incidence of depression and CCMDs in persons with malaria will be presented by continents and study design. Meta-regression analysis will be reported as absolute differences (per 1000) in the overall probability of depression and CCMDs.

Potential amendments

The review of the protocol commenced in 2020 and the study is expected to be completed by 2021. No amendments to this protocol are foreseen; however, in case a need for amendment should arise, it will be registered and reported.

Patient and public involvement

Patients were not involved in the development of this systematic review protocol.

Conclusion

This meta-analysis will include studies with cohort and cross-sectional designs and delineate the risk of depression and common comorbid mental disorders in people with malaria and its neurological complications. To our knowledge, it will be the first comprehensive systematic review and meta-analysis to synthesize the current literature on the prevalence or incidence of depression and CCMDs in persons with malaria. The expected findings will contribute to identifying high-risk populations and will further our understanding of the psychosocial implications of a malarial infection.

Declarations

Dissemination

The results of this systematic review and meta-analysis will be presented at conferences and published in a peer-review journal. The results will additionally guide future population-specific interventions regarding malaria and mental illness.

Contributors

AS and YY conceived this study. YY, MC, and YP drafted the manuscript. AS, YP, MC, VMC critically reviewed the manuscript and provided comments. All authors approved the final manuscript.

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Competing interests

None declared.

Patient consent for publication

Not required.

Abbreviations

CCMDs: common comorbid mental disorders

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Supplementary Files

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- ProtocolPRISMAPchecklist.doc