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The potential of addressing asymptomatic malaria in the context of malaria elimination in Ethiopia: Scoping review

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ABSTRACT

Objectives: Currently, evidence synthesis targeting asymptomatic malaria infections in Ethiopia are scarce. This review intended to collect and organize information on asymptomatic malaria.
Methods: A Joanna Briggs Institute, scoping review protocol was used. Searches for peer-reviewed articles published between 01 January 2010 and 10 August 2022, were done through a variety of databases, and gray literatures.
Results: 17 articles were included out of 7672 articles identified. There was no any longitudinal study to trace forward these asymptomatic malaria cases. The reviewed studies did not address how asymptomatic malaria could be treated. Moreover, living in index houses, their neighbours and family sizes were the main predictors and more associated with onward transmission of malaria. Asymptomatic malaria (ASM) infection might persist in all seasons except June–August, for which data is lacking.
Conclusions: Therefore, as implication of research and policy, it would be necessary to focus on index families and their neighbours in prevention of ASM, conducting longitudinal studies to ascertain when and how many asymptomatic malaria cases without fever during diagnosis would develop clinical malaria. As well, establishing a more sensitive diagnostic technique of malaria surveillance. It is also necessary to provide information regarding the feasibility of treating asymptomatic malaria cases in Ethiopia.

1. Introduction

As countries around the world plan towards eliminating malaria, it would be important to reach out to all infected individuals who are at risk of malaria transmission [1]. An asymptomatic person must be accurately diagnosed and effectively treated in addition to clinical malaria cases [2]. Asymptomatic malaria (ASM) refers to a person harbouring blood-stage malaria parasites who has not experienced fever or other symptoms that would lead the individual to seek treatment [3]. The ASM is commonly reported when the transmission of malaria reaches very low levels, in which the sub-microscopic carriers are the source of 20–50% of all human-to-mosquito transmissions [3]. Of particular concern are asymptomatic carriers who carry gametocytes, which are potentially infectious [2]. Targeting both the clinical and ASM, could help the national malaria elimination program for the country-wide interruption of local mosquito-borne transmission; which can result in reduction to zero incidences of malaria cases [1,4]. Locating asymptomatically infected people and clearing this parasite reservoir will be critical to a sustainable local and national malaria elimination program [1,5].

Ethiopia is among one of the few countries on track to meet the targets set by WHO, by reduction of malaria cases and deaths, over the past two decades [6]. The national malaria elimination program is unlikely to be achieved without addressing ASM and improving the malaria elimination program in Ethiopia. Towards this, malaria endemic areas in Ethiopia were classified as low, moderate, and high malaria burden in 2017 [7]. One of the challenges in low-endemic areas approaching elimination is the widespread presence of asymptomatic Plasmodium infections, which are typically low-density. These infections might help maintain the reservoir of infection and therefore need to be targeted in intervention efforts during the transition from control to elimination [8]. This scoping review would help as a tool for evidence-informed decision-making for researchers, policymakers and program implementers of malaria.

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However, the evidence that supports targeting these is scarce, and also that if we have to target them the most important question that needs to be addressed is the availability of resources in endemic settings. A scoping review is appropriate here as we sought to characterize the body of evidence on ASM through a set of broad research questions.

Therefore, the aim of this review is to identify and map the research evidences of ASM, in terms of key concepts underpinning ASM, diagnostic criteria, and treatments for ASM so far in use in Ethiopia. We conducted a preliminary search of the International Prospective Register of Systematic Reviews (PROSPERO), the Cochrane Database of Systematic Reviews, and the Jonna Briggs Institute (JBI)-Database of Systematic Reviews and Implementation Reports to see if there was already a review on this topic. We did not find any scoping reviews conducted in Ethiopia or elsewhere. Therefore, this scoping review would be important to provide research evidence that could be important for future planning of research or practice in tackling ASM in Ethiopia.

2. Methods

We conducted a systematic search to identify published literatures following the principles and practices of JBI scoping review. The participant, concept and context (PCC) approach was used throughout the review process [9].

We searched for PubMed/MEDLINE database, and Scopus on 9 August 2022. While, we searched for Advanced Google Scholar, WHO malaria library, and ProQuest- Dissertations from 10 to 11 August 2022.

2.1. Search strategy and selection criteria

The search strategy aimed to find both published and unpublished studies [Annex 1]. A three-step search strategy was utilized in this review [10]. An initial limited search of PUBMED has been undertaken, followed by analysis of the text words contained in the title and abstract, and of the index terms used to describe the article. A second search using all identified keywords and index terms was conducted across all included databases. Thirdly, the reference lists of all identified articles were searched for additional studies. We searched articles published in English from 2010 to 2022 for inclusion in this review.

We searched for PUBMED/MEDLINE and Scopus databases for the search of published research articles and we searched through gray literature reports (unpublished studies) through WHO malaria library, Google scholar and ProQuest- Dissertations. We used asymptomatic malaria, malaria control, malaria elimination, sub-microscopic malaria, polymerase-chain reaction (PCR), and of Loop-mediated-isothermal amplification (LAMP) as initial keywords.

Following the search, all the identified citations were collated and uploaded into the EndNote X7(build 7072) system and duplicates were removed. Titles and abstracts were then screened by two independent reviewers for assessment against the inclusion criteria for the review. Studies that met the inclusion criteria were retrieved in full after screening of titles and abstracts by two independent reviewers. Full details of the articles were also reviewed by two independent reviewers and assessed against the inclusion criteria. Any disagreement that rose between the two reviewers was resolved at each step of the study selection process through discussion.

Full-text studies that do not meet the inclusion criteria were excluded with reasons, and the included studies and the results of the search was reported in full and presented in a Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews (PRISMA-ScR) flow diagram [11] and PRISMA-ScR checklist was attached in Annex 4[11]

2.2. Data extraction and analysis

Data was extracted from papers included in the review using the data extraction tool available in JBI scoping review. The extracted data included specific details about the population; concept and context (PCC). Studies with any age category dealt with ASM were included. The starting year was selected, because, ASM researches was initiated in Ethiopia in 2010 [12]. All studies conducted in any geographical setups of Ethiopia, or any health facility type or households, or schools, blood banks and articles in English were included in this review [Fig. 1].

2.3. Included studies

The initial search retrieved 7649 articles through database searches and 23 additional records identified through other sources, of which 538 articles were excluded due to duplications. The titles and abstracts were the exclusion criteria for the articles in the second stage. Accordingly, 7134 research articles, which don't have any connection to the objective of the review of the title and abstracts, were excluded in the screening process. In the next stage, any study of doubt was assessed for full-text eligibility and the full-text for 30 studies were assessed and another nine studies were removed with reasons of not dealt with ASM and the full text was not available for four studies and seventeen studies were finally included in the review [Fig. 1].

Only primary research studies were included in accordance with the aim of the review to avoid double-reports from primary and review studies. All cross-sectional, longitudinal, and randomized clinical trials studies were included, however, protocols and reviews were excluded. We didn't approach authors to get unpublished studies/gray literatures. The included and excluded research articles were presented through PRISMA flow diagram indicated in [Fig. 1] and PRISMA-ScR [annex 4].

2.4. Data extraction

The extracted research articles and the data needed for our scoping review were presented in a logical and descriptive summary aligned with the objectives of the review. Criteria for data extraction were determined by creating a checklist consisting of author's surname, study design, study population and season/month of the study period (Table 1). The scoping review results were also presented in relation to the diagnostic criteria used to define ASM, and the associated factors of ASM were given in [Annex 2].

3. Result

3.1. Presentation and charting of results

The extracted data was analysed descriptively and the result was presented using a PRISMA figure and tables, to ensure adequate visualization of the key findings. Research evidences of ASM were organized based on the objectives of the review. Then the review was framed in to three thematic focuses of; the laboratory diagnostic methods used, the ASM and associated factors, and treatment of ASM.

3.2. Characteristics of the included studies

Table 1 was about the characteristics of seventeen studies, which were eligible and being included in the review. Sixteen of the studies were cross-sectional study designs and and cluster-randomized trial. Six studies were conducted in Oromia region, five from Amhara region, and three from Southern Nations, Nationalities, and Peoples' Region (SNNPR) and three from the national study. Eight studies were carried out in health facility and another six in the community, as well as two in the school and one in the blood bank. The target groups of the included studies were school and preschool children, pregnant women, blood donors and adults.

All included articles were published in English between 2010 and 2022 [12–21]. Eight of the included research articles were conducted during peak malaria transmission seasons in Ethiopia (from September to December and from March to May). Whereas nine of the research

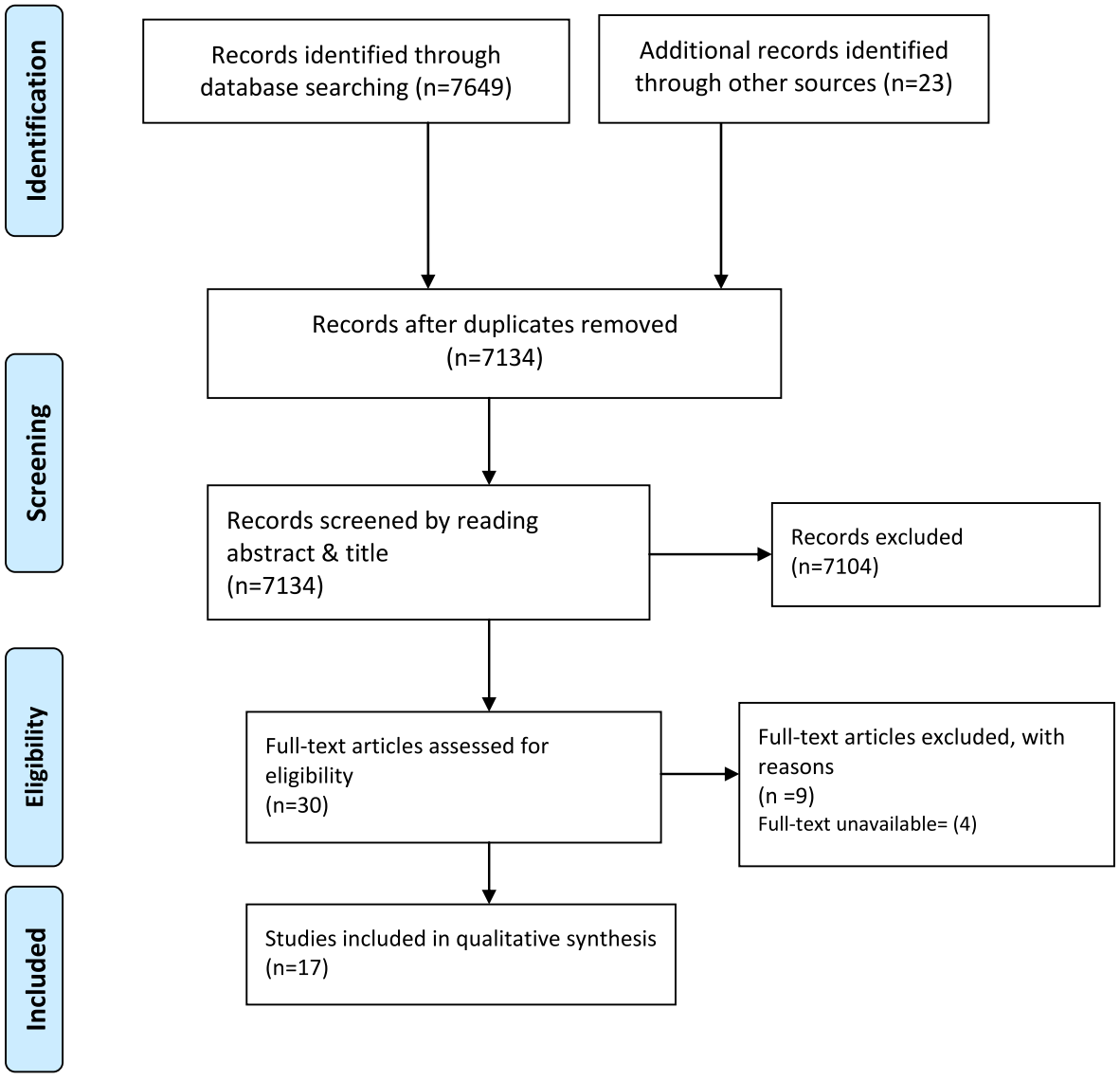

Fig. 1. PRISMA flow diagram of search results and study selection and inclusion process (11).

articles were conducted at different times as they dealt with members and neighbours of index malaria cases, blood donors, and pregnant women, [13,14,18]. In this review, ASM infection can persist in all seasons except June–August (for which no research data was found).

3.3. Laboratory diagnostic methods of ASM in Ethiopia

All the included articles dealing with ASM defined it as the detection of asexual or sexual malaria parasites and the absence of any clinical symptoms of malaria, usually fever, for a specified period of time. Microscopy, rapid diagnostic test (RDT), and polymerase chain reaction (PCR) were used as diagnostic tools for ASM in eight (47%) of the included studies. Microscopy and RDT were used in four (23.5%) of the studies, and microscopy alone was used in four (23.5%) of the studies, and microscopy and LAMP were used in only one study. None of the included studies were traced back to these ASM cases to know how many without fever at the time of the diagnosis will develop clinical malaria in the future. None of the included studies involved the use of next-generation sequencing (NGS).

3.4. Associated factors with ASM in Ethiopia

The prevalence of ASM varied across different geographical settings and target groups in Ethiopia. The highest prevalence of sub-microscopic malaria was 19.2% among individuals of age ≥ two years of age in West Arsi Zone, Shalla District of Oromia Region [12]. The second highest prevalence of 17.5% was reported among individuals living among households of index cases [13]. Similarly, the prevalence of ASM among apparently healthy pregnant women in the city of Arbaminch was 9.1% [18].

In addition, the prevalence of ASM among blood donors was 4.1% in Arbaminch town in SNNPR [14] and 6.8% among school children in Dembia district in North Ethiopia. respectively [16]. In terms of species, 92.59% of the PCR-detected RACD cases were *P. falciparum* and the remaining 7.41% were *P. vivax* [13]. In addition,Golassa (2015) reported a total microscopy positive samples of; 45%, 40% and 14.5 % for *P. falciparum, P. vivax*, and mixed infections, respectively from an apparently healthy individuals of age greater than or equal to two years [17]. In terms of the parasitic load, Alemu (2018) reported, that 16 out of 17 (94%) positive blood films showed a light infection of fewer than 1000 parasites/μl of blood [14].

According to Tadesse (2018), membrane feeding experiments, ASM

Table 1
Summary of the included (n = 17).

Author	Study population	Study design	Diagnostic methods	Sample size(n)	Seasons, years	Description of Study population, follow up duration, if any
Golassa et al. 2013 [12]	HHs	Cross-sectional	Microscopy, RDT, PCR	1453 individuals	February	Age ≥ years, with no known acute &/or, no history of fever in the last 72 h
Zemene et al. 2018 [13]	IC &HHs in index	Cross-sectional	Microscopy, RDT, PCR	726 individuals	NA	Screening of all family members & neighbours of index-case
Alemu et al. 2014 [14]	Blood donors	Cross-sectional	Microscopy	416 blood donors	NA	Blood donors Age>18
Girma F [15]	HHS, clinics	Cross-sectional	Microscopy, PCR	490 individuals	September mid -November and April to May	ASM (community), clinical patients Age> 2
Fekadu, Yenit, and Lakew 2018 [16]	HHs	Community- based cross-sectional	Microscopy, RDT	832 individuals	October 11 to Nov 2017	Adults included in the study
Golassa et al. 2015 [17]	Clinical & subclinical pts	Cross-sectional	Microscopy, RDT, PCR	1094 individuals	November–December 2015	Apparently healthy individuals≥ 2 years
Nega et al., 2015 [18]	pregnant women	Community-based cross-sectional	Microscopy	341 pregnant women	February–march 2013	Any pregnant women visited health facility during the study
Ligabaw W. (2015) [19]	School children	Cross-sectional	Microscopy	385 school children	NA	School-aged children,6–15 years
Tadesse et al. 2017 [20]	HHs	Community-based cross-sectional	Microscopy, RDT, PCR	–	October–December 2017	All age groups
Assefa et al., 2020 [21]	All age groups	cross-sectional survey	Microscopy, RDT, PCR	2608 individuals	September–December 2020	All age groups from the Ethiopian Malaria Indicator Survey 2015 (EMIS-2015)
Limenih 2021 [22]	Delivering mothers	Cross-sectional	Microscopy	218 delivering mothers	February to May 2021	Delivering mothers without sign & symptoms of malaria
Subussa et al. 2021 [23]	pregnant women	cross-sectional	Microscopy, RDT	–	March to September 2018	Pregnant women without sign & symptoms of malaria
Leonard et al. 2022 [24]	All age groups	cross-sectional survey	Microscopy, RDT, PCR	2648 individuals	September–December 2015	All age groups from the Ethiopian Malaria Indicator Survey 2015 (EMIS-2015)
Feleke, 2021 [25]	pregnant women	Cross-sectional study	Microscopy, RDT,LAMP	263 pregnant women	from November 2018 to January 2019	Pregnant women with the absence of disease symptom/sign within the past 48 h
Hailemeskel et al. 2021 [26]	Afebrile and apparently healthy individuals	cross-sectional surveys	Microscopy, RDT, PCR	1093 individuals	NA	Afebrile and apparently healthy individuals,
Tadesse et al. 2020 [27]	Pregnant women	Cross-sectional	Microscopy, RDT, PCR	199 pregnant women	September to December	Pregnant women with & without any clinical symptoms,
Zerdo et al. 2021 [28]	School-aged children	Cluster-randomized trial	Microscopy, RDT	2167 children	October and December 2019	School children without any clinical symptoms

Key: ASM = Asymptomatic malaria = sample size, HHs = house-hold, NA=Not applicable, SNNP= Southern Nations, Nationalities, and Peoples (SNNPS), IC = index cases.
RDT = Rapid-diagnostic-test, PCR = polymerase-chain-reaction, LAMP = Loop-mediated-isothermal-amplification, NGS=Next generation sequencing.

was responsible for the majority of onward mosquito infections. Clinical *P. vivax*, asymptomatic microscopy- or PCR-detected infections were responsible for 8.0%, 76.2% and 15.8% of the infectious reservoir, respectively, while *P. falciparum was responsible for* 0.8%, 69.5% and 29.7% of the infectious reservoir in the case of Clinical *malaria*, asymptomatic microscopy- or PCR-detected infections, respectively [15].

The prevalence of asymptomatic parasitemia, in turn, was significantly associated with not using bed net, gender, with males being 6.7% more likely than females to be at risk of ASM, and adults over 35 years of age had the lowest microscopically determined infection rates of 2.4%, and individuals of age groups of 15–19 years were 4.5 times more likely to have ASM [14,17,19]. Travelling away from residence area and living closer to stagnant water had a 5-fold and 3.7-fold greater likelihood of getting ASM infections [16]. Living in index houses and family sizes were the main predictors and more associated with the onward transmission of malaria [13].

4. Discussion

Research articles conducted in four regional governments of Ethiopia and one national based study were included. These regions have different geo-ecological settings of high, medium and low altitudes, which can favour the transmission of malaria. Data could vary between transmission strata of the country as the country has varying malaria endemicities of high, moderate low to very low [4,6].

16 (94%) of the included studies were cross-sectional studies and one randomized controlled trial (RCT). As a result, nothing was known, about, how much of those no measured fever after the time of diagnosis, was developed the clinical malaria, after a certain period of time [12–14,17,19,21–28]. In addition, Microscopy, RDT and PCR were used as the main diagnostic tools in this review. However, only one of the included studies used the loop-mediated-isothermal amplification (LAMP) technique, for ASM as a confirmatory diagnostic tool [25].

The extent of ASM has not been well studied with large sample sizes from nationwide population surveys in Ethiopia. There have also been controversies in studies about the target group of ASM. According to a community study conducted by Lemu (2015), children under 5 years had higher ASM of 12.7% [17], while according to Ligabaw (2014), ASM was highest (15.1%), among school children aged 6 to 10 (19), and according to a community study conducted by Mesafint (2017), people aged 15–49 years are four to five times more likely to contract malaria [16].

According to Endalew (2018), the prevalence of malaria among index house residents and their neighbours was 17.5% and 6.83%, respectively. At the same time, living in the index case house was twice as likely to be associated with ASM [13]. However, it would be necessary to know how many ASM cases were expected/estimated for malaria, considering the different malaria endemicties of low, medium and high [3,8,13]. Furthermore, none of the included studies addressed public

health interventions how ASM could be treated [12–28].

In countries like Ethiopia where both malaria spps predominate, other important factors could also play paramount role in determining the occurrence of ASM. Most *P. vivax* infections detected in community surveys or at the health system are often related with relapsing episodes, up to 72% [29]. This is the result of the presence of a dormant liver stage for which no diagnostics exists to-date. A community intervention that is based on screening and treatment could not find these infections. The other important difference between the two species is the already lower parasite density for *P. vivax* related with its strict preference to infect only young RBCs [29]. These biological differences could challenges of malaria elimination in setting sympatric to both species, like Ethiopia. Moreover, the occurrence of malaria is determined by age of the human host, transmission intensity, vector composition and competency to transmit low density infections.

The prevalence of ASM was increased among those who never used insecticide-treated nets and were living near stagnant water by six and three times, respectively [30] and ASM infection was 1.54 times higher in primigravida women compared to multigravida women. ASM infected pregnant women were 2.28 times more likely anemic than non-infected pregnant women [31].

None of the included studies addressed the public health interventions, how ASM might be managed and treated at the health facility and community levels [Annex 2]. Under such conditions, it would be better to discuss the global experience of management and treatment of ASM. There are currently three approaches to treating ASM [WHO,2010]. First, WHO recommends the use of intermittent preventive therapies (ITP)-interventions that address the repeated treatment of high-risk groups with antimalarials that are not guided by diagnostic testing for infants ages 10, 14 weeks, and 9 months, and Pregnant women from the second trimester and can be administered at monthly intervals until delivery [WHO ITP,2010]. Second, Mass Drug Administration (MDA) provides antimalarial drugs to the population in a given geographic area, regardless of their infection or symptom status [WHO MDA, 2015]. The third option is Mass Screening and Treat (MSaT), in which the population is comprehensively screened with a malaria diagnostic test and infected cases are treated [WHO Global Malaria Programme, 2015].

In this review, ASM infection can persist in all seasons except June–August (for which no research data was found). This suggests that a significant portion of the population remains parasitic year-round, even when clinical malaria cases are few during Ethiopia's dry seasons. This reassures that malaria transmission can occur in areas where clinical cases of malaria have been monitored and treated. The invisible malaria transmissions, might responsible for the ongoing malaria outbreaks.

5. Risk of bias across studies

Not applicable (NA) for scoping review.

6. Limitations of the scoping review

6.1. Limitation of the study

We have included PUBMED/Medline, and Scopus databases for searching of published research articles in this scoping review and couldn't get and EMBASE database access. Due to this, the number of available published ASM research articles in Ethiopia, might be higher than the number of research articles included in this Scoping review. As well, expert opinion of policy-makers, researchers or any stakeholders was not included in to this scoping review.

7. Conclusions

The review revealed several gaps in the literature that are worth exploring in future research. All of the included studies were cross-sectional study designs, except one randomized controlled trial (RCT). Most of the included studies assessed the extent of ASM in preschool, school children, pregnant women, blood donors and adults. The prevalence of ASM was high among households of index cases and their neighbours. Therefore, as implication of research and policy, it would be necessary to focus on index families and their neighbours in prevention of ASM, conducting longitudinal studies to ascertain when and how many asymptomatic malaria cases without fever during diagnosis would develop clinical malaria. As well, establishing a more sensitive diagnostic technique of malaria surveillance. It is also necessary to provide information regarding the feasibility of treating asymptomatic malaria cases in Ethiopia. In addition, it is important to know how much ASM could be detected in a specific malaria endemic environment of low, medium and high endemicities. Particularly, looking the feasibility of treating ASM cases in children and pregnant women and conducting a nationwide survey, to know the burden of ASM in different malaria endemic areas in Ethiopia.

Ethics approval and consent to participate

Not Applicable, as it is a review.

Availability of supporting data

All data generated and analysed in this review were from original articles. Numbers of articles included and rejected for this review were indicated in PRISMA table as well in [Annex 3].

Authorship

DA and SD contributed in the conception and design of the study, searching, screening, data extraction, analysis and write-up. While, AA and LG involved in final revision of the scoping review and all authors read and approved the final manuscript.

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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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List of abbreviations

ASM-Asymptomatic malaria, LAMP-Loop-Mediated Isothermal Amplification. PCR-Polymerase Chain Reaction. JBI-Jonna Briggs Institute. PRISMA-Preferred Reporting Items for Systematic-Review & Meta-analysis. WHO-World Health Organization.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.puhip.2023.100454.

References

[1] World Health Organization and Global Malaria Programme, A Framework for Malaria Elimination, 2017. Geneva, http://apps.who.int/iris/bitstream/handle/10665/254761/9789241511988-eng.pdf?sequence=1/. (Accessed 10 August 2022).

[2] The Global health group, A Guide on Malaria Elimination for Policy Makers, 2009. http://www.malariaeliminationgroup.org/publications/shrinking-malaria-map-guide-malaria-elimination-policy-makers/ [accessed 10 August 2022].

[3] L. Okell, B. Teun, G. Jamie, O. André Lin, C.G. Azra, J.D. Chris, Factors determining the occurrence of sub-microscopic malaria infections and their relevance for control, Nat. Commun. 3 (2012) 1–9, https://doi.org/10.1038/ncomms2241.

[4] Federal Democratic Republic of Ethiopia Ministry of Health, National Malaria Elimination Roadmap. Addis Ababa, 2017 (13) (PDF) Malaria Elimination Roadmap in Ethiopia (researchgate.net). (Accessed 10 August 2022).

[5] T.L. Jessica, L.S. David, R.M. Steven, The role of sub-microscopic malaria in malaria transmission: what is the evidence? Trends Parasitol. 30 (4) (2014) 183–190. https://doi:10.1016/j.pt.2014.02.004.

[6] Federal Democratic Republic of Ethiopia Ministry of Health, National malaria elimination strategic plan, Addis Ababa (2022) Ethiopia malaria elimination strategic plan: 2021-2025 (moh.gov.et)/ (Accessed 11 August 2022);1-76.

[7] D. Nega, A. Abera, B. Gidey, S. Mekasha, A. Abebe, D. Dillu, D. Mehari, Baseline malaria prevalence at the targeted pre-elimination districts in Ethiopia, BMC Publ. Health 21 (1) (2021) 1–11, https://doi.org/10.1186/s12889-021-12036-5.

[8] World Health Organization, World Health, Policy brief on malaria diagnostics in low-transmission settings. Geneve. https://www.who.int/publications-detail-redirect/WHO-HTM-GMP-2014.4/;2014. (Accessed 11 August 2022).

[9] E. Aromataris, Z. Munn, JBI Manual for Evidence Synthesis, JBI, 2020, https://doi.org/10.46658/JBIMES-20-01 synt hesis manual.jbi.global.

[10] E. Aromataris, Z. Munn, Introduction to scoping reviews, JBI 2020" JBI Manual. Evid. Synt. 21 (2018) wiki.jbi.global/display/MANUAL/11.1+Introduction+to+Scoping+reviews.

[11] D. Moher, A. Liberati, J. Tetzlaff, D.G. Altman, The PRISMA Group.Preferred reporting Items for systematic reviews and meta- analyses: the PRISMA statement, PLoS Med. 6 (7) (2009), e1000097, https://doi.org/10.1371/journal.pmed.1000097.

[12] L. Golassa, N. Enweji, B. Erko, A. Aseffa, G. Swedberg, Detection of a substantial number of sub- microscopic Plasmodium falciparum infections by polymerase chain reaction : a potential threat to malaria control and diagnosis in Ethiopia, Malar. J. 12 (1) (2013) 1, https://doi.org/10.1186/1475-2875-12-352.

[13] Z. Endalew, C. Koepfli, A. Tiruneh, K.Y. Asnakew, D. Seyoum, M.C. Lee, G. Yan, D. Yewhalaw, Detection of foci of residual malaria transmission through reactive case detection in Ethiopia, Malar. J. 17 (1) (2018) 1–10, https://doi.org/10.1186/s12936-018-2537-5.

[14] A. Alemu, H.P. Fuehrer, G. Getnet, A. Kassu, S. Getie, H. Getie, Comparison of Giemsa microscopy with nested PCR for the diagnosis of malaria in North Gondar, North-west Ethiopia, Malar. J. 13 (2014) 174, https://doi.org/10.1186/1475-2875.

[15] Tadesse FG, Slater HC, Chali W, Teelen K, Lanke K, Belachew M.et al. The relative contribution of symptomatic and asymptomatic *Plasmodium vivax* and *Plasmodium falciparum* infections to the infectious reservoir in a low-endemic setting in Ethiopia, January2018: 1–26 (unpublished document). https://doi.org/10.1093/cid/cix1123/4786592.

[16] M. Fekadu, K.M. Kindie, A.M. Lakew, The prevalence of asymptomatic malaria parasitemia and associated factors among adults in Dembia District, Northwest Ethiopia, Arch. Publ. Health 76 (1) (2017) 1–6, https://doi.org/10.1186/s13690-018-0323-z.

[17] L. Golassa, F.N. Baliraine, N. Enweji, B. Erko, G. Swedberg, A. Aseffa, Microscopic and molecular evidence of the presence of asymptomatic Plasmodium falciparum and Plasmodium vivax infections in an area with low, seasonal and unstable malaria transmission in Ethiopia, BMC Infect. Dis. 15 (1) (2015) 1–10, https://doi.org/10.1186/s12879-015-1070-1.

[18] D. Nega, D. Dana, T. Tefera, T. Eshetu, Prevalence and predictors of asymptomatic malaria parasitemia among pregnant women in the rural surroundings of Arbaminch town, south Ethiopia, PLoS One 10 (4) (2015), e0123630, https://doi.org/10.1371/journal.

[19] L. Worku, D. Damtie, M. Endris, S. Getie, M. Aemero, Asymptomatic malaria and associated risk factors among school children in Sanja town, Northwest Ethiopia, Int. Sch. Res. 2014 (2014) 1–6.

[20] F.G. Tadesse, L.V. den Hoogen, K. Lanke, K. Schildkraut, K. Tetteh, A. Aseffa, et al., The shape of the iceberg: quantification of submicroscopic *Plasmodium falciparum* and *Plasmodium vivax* parasitaemia and Gametocytaemia in five low endemic settings in Ethiopia, Malar. J. 16 (1) (2017) 1–11, https://doi.org/10.1186/s12936-017-1749-4.

[21] A. Assefa, A. Ahmed, W. Deressa, G.G. Wilson, A. Kebede, H. Mohammed, Assessment of sub-patent Plasmodium infection in North-western Ethiopia, Malar. J. 19 (1) (2020) 1–10, https://doi.org/10.1186/s12936-020-03177-w.

[22] A. Limenih, W. Gelaye, G. Gelaye, Prevalence of malaria and associated factors among delivering mothers in Northwest Ethiopia, BioMed Res. Int. 1–7 (2021), https://doi.org/10.1155/2021/2754407.

[23] B.W. Subussa, T. Eshetu, T. Degefa, M.M. Ali, Asymptomatic Plasmodium infection and associated factors among pregnant women in the Merti district, Oromia, Ethiopia, PLoS One 16 (3) (2021), e0248074, https://doi.org/10.1371/journal.pone.0248074.

[24] C.M. Leonard, A. Assefa, J.N. McCaffery, C. Herman, M. Plucinski, S. Plucinski, Investigation of Plasmodium falciparum Pfhrp2 and Pfhrp3 gene deletions and performance of a rapid diagnostic test for identifying asymptomatic malaria infection in Northern Ethiopia, Malar. J. 21 (1) (2022) 1–9, https://doi.org/10.1186/s12936-022-04097-7.

[25] D.G. Feleke, Y. Alemu, N. Yemanebirhane, "Performance of rapid diagnostic tests, microscopy, loop-mediated isothermal amplification (LAMP) and PCR for malaria diagnosis in Ethiopia: a systematic review and meta-analysis, Malar. J. 20 (1) (2021) 1–11, https://doi.org/10.1186/s12936-021-03923-8.

[26] E. Hailemeskel, S. Tebeje, S.W. Behaksra, G. Shumie, G. Shitaye, The epidemiology and detectability of asymptomatic Plasmodium vivax and Plasmodium falciparum infections in low, moderate and high transmission settings in Ethiopia, Malar. J. 20 (1) (2021) 1–10, https://doi.org/10.1186/s12936-021-03587-4.

[27] G. Tadesse, C. Kamaliddin, C. Doolan, R. Amarasekara, R. Legese, A.N. Mohon, Active case detection of malaria in pregnancy using loop-mediated amplification (LAMP): a pilot outcomes study in South West Ethiopia, Malar. J. 19 (1) (2020) 1–9, https://doi.org/10.1186/s12936-020-03380-9.

[28] Z. Zerdo, H. Bastiaens, S. Anthierens, F. Massebo, M. Masne, G. Biresaw, Prevalence and associated risk factors of asymptomatic malaria and anaemia among school-aged children in dara mallo and uba debretsehay districts: results from baseline cluster randomized trial, Malar. J. 20 (1) (2021) 1–12, https://doi.org/10.1186/s12936-021-03937-2.

[29] R.N. Prasad, K.J. Virk, V.P. Sharma, Relapse/reinfection patterns of Plasmodium vivax infection: a four year study, Southeast Asian J. Trop. Med. Publ. Health 22 (4) (1991) 499–503. PMID: 1820634.

[30] Y. Yimam, M. Nateghpour, M. Mohebali, M.J. Abbaszadeh Afshar, A systematic review and meta-analysis of asymptomatic malaria infection in pregnant women in Sub-Saharan Africa: a challenge for malaria elimination efforts, PLoS One (4) (2021) 16.

[31] A. Tamiru, T. Tolossa, B. Regasa, G. Mosisa, Prevalence of asymptomatic malaria and associated factors in Ethiopia: systematic review and meta-analysis, SAGE Open Med 10 (2022) 1–17.