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Prevalence of thrombocytopenia among patients with malaria in Ethiopia: a systematic review and metanalysis

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Abstract

Background Thrombocytopenia is a common haematological abnormality in malaria patients that is associated with an increased risk of mortality. Given the endemic nature of malaria in Ethiopia, it is crucial to comprehend the prevalence of thrombocytopenia in this setting to enhance clinical care. Therefore, this study aimed to systematically review and synthesize the available evidence on the prevalence of thrombocytopenia among malaria patients in Ethiopia.

Methods This systematic review and meta-analysis reviewed studies on thrombocytopenia prevalence in malaria patients, using databases including PubMed, Google Scholar, EMBASE, African Journals online database, and Hinary. STATA version 17 software was used for statistical analysis. A random-effects model was used to estimate pooled effect sizes. Heterogeneity among the included studies was assessed using Galbraith, Cochran's Q test, and I^2 statistics. Subgroup analysis, sensitivity analysis, and meta-regression were conducted to identify the source of heterogeneity. Publication bias was evaluated using a funnel plot and Egger's test.

Results Of the 154 studies identified, 31 that fulfilled the eligibility criteria were included in the meta-analysis consisting of 1173 study participants and 823 thrombocytopenic cases. The pooled prevalence of thrombocytopenia was 70% (95% CI: 63, 77) with significant heterogeneity. Subgroup analysis showed the highest pooled prevalence of thrombocytopenia in the Southern Nations Nationalities and Peoples' region (78.34%) followed by the Amhara region (69.7%), whereas the lowest prevalence was observed in the Gambella Region (63.4%). The sample size was responsible for the observed heterogeneity among the studies, as indicated by the statistically significant result in the meta-regression analysis ($p = 0.001$).

Conclusion Thrombocytopenia is a frequent abnormality finding among malaria patients in Ethiopia, affecting a substantial percentage of individuals. The high frequency found in this research emphasizes the significance of regular platelet monitoring in the treatment of malaria patients. Further studies are needed to investigate the clinical implications of thrombocytopenia in malaria patients.

Keywords Malaria, Thrombocytopenia, Platelet count, Plasmodium infections, Hematological abnormalities, Ethiopia

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Background

Malaria, a mosquito-borne infectious disease primarily caused by *Plasmodium falciparum* and *Plasmodium vivax*, continues to be a major public health problem in some developing countries, including Ethiopia, resulting in significant annual deaths in the world [1]. According to the World Health Organization (WHO), over 7.3 million malaria cases and 1157 deaths (0.02%) of case fatality rate) were reported in Ethiopia between 1 January and 20 October 2024 [2]. Malaria can lead to a variety of complications including neurological complications, organ damage, metabolic disturbances, haematological abnormalities, and finally death. Thrombocytopenia, defined as a reduced platelet count (150,000/ µl), is a common haematological complication observed in patients with malaria [3].

Due to its strong associations with malaria, thrombocytopenia sometimes serves as a clinical marker for suspicion of malaria in patients with acute febrile illnesses, often in malaria-endemic areas [4, 5]. It serves as a suggestive for a severe disease course and requires prompt and aggressive treatment. Thrombocytopenia can contribute to a range of clinical issues, including an increased risk of haemorrhagic complications [6]. In severe forms, it may lead to spontaneous bleeding, complicates disease management, and has higher mortality rates, making it a critical factor in patient prognosis and diagnostic clues in endemic regions [7, 8]. Although the exact cause of thrombocytopenia in malaria is unknown, probable causes may include increased platelet consumption or destruction; decreased thrombopoiesis; or a combination of coagulation abnormalities, oxidative stress, splenomegaly, bone marrow abnormalities, and platelets' involvement as cofactors in causing severe malaria [9–11]. Additionally, antibody-mediated platelet destruction, where the immune system produces antibodies that bind to platelets, exacerbates the depletion of platelets in malaria patients, is another possible mechanism [12].

The frequency of thrombocytopenia in malaria patients could vary depending on different factors including disease severity, malaria species, geographical area, and other individual-level factors. It could range from 40% to over 80%, with higher rates in severe cases of *P. falciparum* infection [13–15]. Species-specific differences include *P. falciparum* being more frequently associated with thrombocytopenia compared to *P. vivax* [16]. Extreme age groups and immunocompromised individuals are more likely to experience thrombocytopenia [17]. Thrombocytopenia prevalence also varies by region, with sub-Saharan Africa showing higher rates [18]. Severe malaria cases, particularly those requiring hospitalization, often show a higher prevalence of thrombocytopenia, directly correlated to the disease's severity and mortality risk [7].

Although some primary studies have revealed that the burden of thrombocytopenia in malaria patients is high, their results have revealed substantial variation regarding its prevalence [19–21]. Moreover, in Ethiopia, where malaria continues to pose a serious health threat, the frequency of thrombocytopenia in malaria patients has not been systematically assessed across the studies. Given the clinical significance of thrombocytopenia, it is imperative to obtain a thorough understanding of its prevalence in this population to enhance healthcare practices and patient outcomes. This systematic review and metanalysis is therefore aimed to synthesize a comprehensive overview of thrombocytopenia prevalence among malaria patients in Ethiopia based on the existing literature. This could help for a better understanding of the burden of thrombocytopenia, to promote routine platelet monitoring and targeted interventions for high-risk patients.

Methods

Protocol registration and searching strategy

The Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA) 2020 guideline was used to develop the systematic review and meta-analysis was used to report the search process [22] (Supplementary file 1). The protocol was registered by the International Prospective Register of Systematic Reviews (PROSPERO) database with registration identification number CRD42024573404. A thorough search of articles published until July 4, 2024, was conducted using online databases such as PubMed, Hinari, African Journals online database, and EMBASE. Google Scholar and Google were searched to access grey literature. In addition, institutional repositories were also manually searched. The searches were performed by combining different MeSH terms and keywords, including 1. population (malaria patients), 2. outcome (Thrombocytopenia, 'low platelet count", "hematological parameters", platelet count"), 3. context (Ethiopia and different regions of Ethiopia) both in separation and in combination using Boolean Operator (OR, AND). A detailed search strategy is presented in supplementary file 2.

To ensure that all pertinent studies carried out in the field were found, the reference lists of the included studies were also reviewed. Additionally, a manual search and an examination of grey literature were conducted to identify unindexed research publications.

Eligibility criteria

The CoCoPop approach (condition, context, and population), commonly used in systematic reviews of prevalence studies, was employed to define the criteria for including

and excluding studies [23]. After carefully reviewing the articles' content, studies that satisfied the following requirements were included.

Population (Study participants): adults with malaria.

Context Observational studies conducted in Ethiopia.

Condition (outcome of interests): Studies reported the prevalence of thrombocytopenia.

Whereas, review articles, editorial opinions, case reports, letters to the editor, and abstracts from conferences were excluded.

Study outcome(s)

The outcome of this study was the pooled prevalence and 95% confidence interval (95% CI) of thrombocytopenia, which, according to the original publication, was expressed as a percentage or as the number of patients with low platelet counts relative to all participants.

Study selection and data extraction

The selection of articles was independently conducted by two authors (ABK and MSA) in accordance with the predefined inclusion and exclusion criteria. They got in touch with the authors of any articles that were not open access; the articles whose authors did not respond were deleted. Following the identification of all eligible articles, these two independent reviewers (ABK and MSA) extracted the pertinent information using an organized standard data extraction form by Microsoft Excel spreadsheet. The following data items were taken out of each article. author name, study participants, study area, publication year, study design, sample size, number of patients with thrombocytopenia, mean/median platelet count, and *Plasmodium* species. Any disagreement between the reviewers was resolved by discussion to reach a consensus.

Risk of biases

Two independent reviewers (ABK and MSA) initially assessed the methodological quality of the included articles using the Joanna Briggs Institute (JBI) critical appraisal tool for observational studies [24]. Studies with an average quality score higher than fifty percent (50%) were considered as good quality and included in the final analysis (Supplementary file 3). Disagreements between the two reviewers (ABK and MSA) were then resolved through discussion with a third author (A.G).

Data synthesis and analysis

Data were extracted using extraction format and were exported into STATA version 17 for final analysis. A narrative synthesis was used to present the data. The inverse-variance weighting method was applied to weight the effect sizes of the included primary studies. The results of this review were summarized and presented using forest plots, tables, and narrative text. The weighted inverse variance random effect model was used to estimate the pooled effect sizes accompanied by a corresponding 95% CI. Heterogeneity was assessed by graphical methods using the Galbraith plot and forest plot as well as statistically using I^2 test statistics and Cochran's Q test. A p-value of < 0.05 for the Q test I^2 value of $> 25\%$ was considered as the presence of heterogeneity. In this meta-analysis, I2 was found to be high ($> 75\%$) and the Q statistic test was found to be significant, suggesting the presence of heterogeneity and the use of a random effect model. A pre-defined subgroup analysis and meta-regression were performed to identify the source of heterogeneity. A leave-one-out sensitivity analysis was conducted to assess the robustness of the pooled estimates about outliers and to evaluate the influence of individual studies on the overall estimate [25]. In addition, publication bias was assessed visually using funnel plots to check for asymmetry and statistically using Egger's test to detect any significant bias in the included studies [26].

Results

Selection of studies

Initially, 154 studies were identified from database searches and other sources. Of these, 19 were removed due to duplication. The remaining 135 articles were screened based on title and abstract, and 121 were excluded. Ultimately, 14 articles were thoroughly evaluated against the eligibility criteria, and 10 of them were found to be potentially eligible for inclusion in this systematic review and meta-analysis (Fig. 1).

Study characteristics

This study summarized and analysed the results of 10 previous research articles from different parts of Ethiopia. All the included studies were scoring over 50% on quality assessments. The total number of participants across all the studies was 1173, with 823 of them having thrombocytopenia (low platelet count). The highest (84.12%), and the lowest (51.49%) prevalence of thrombocytopenia among malaria patients were reported in studies conducted in SNNP and Oromia region, respectively. All the included studies used a cross-sectional design, where data was collected from healthcare facilities (Table 1).

Prevalence of thrombocytopenia among malaria patients in Ethiopia

The prevalence of thrombocytopenia among malaria patients ranged from 51.49% in Adama, Oromia to 84.12% in Tercha, SNNP. The random effect model analysis revealed that the overall pooled prevalence of

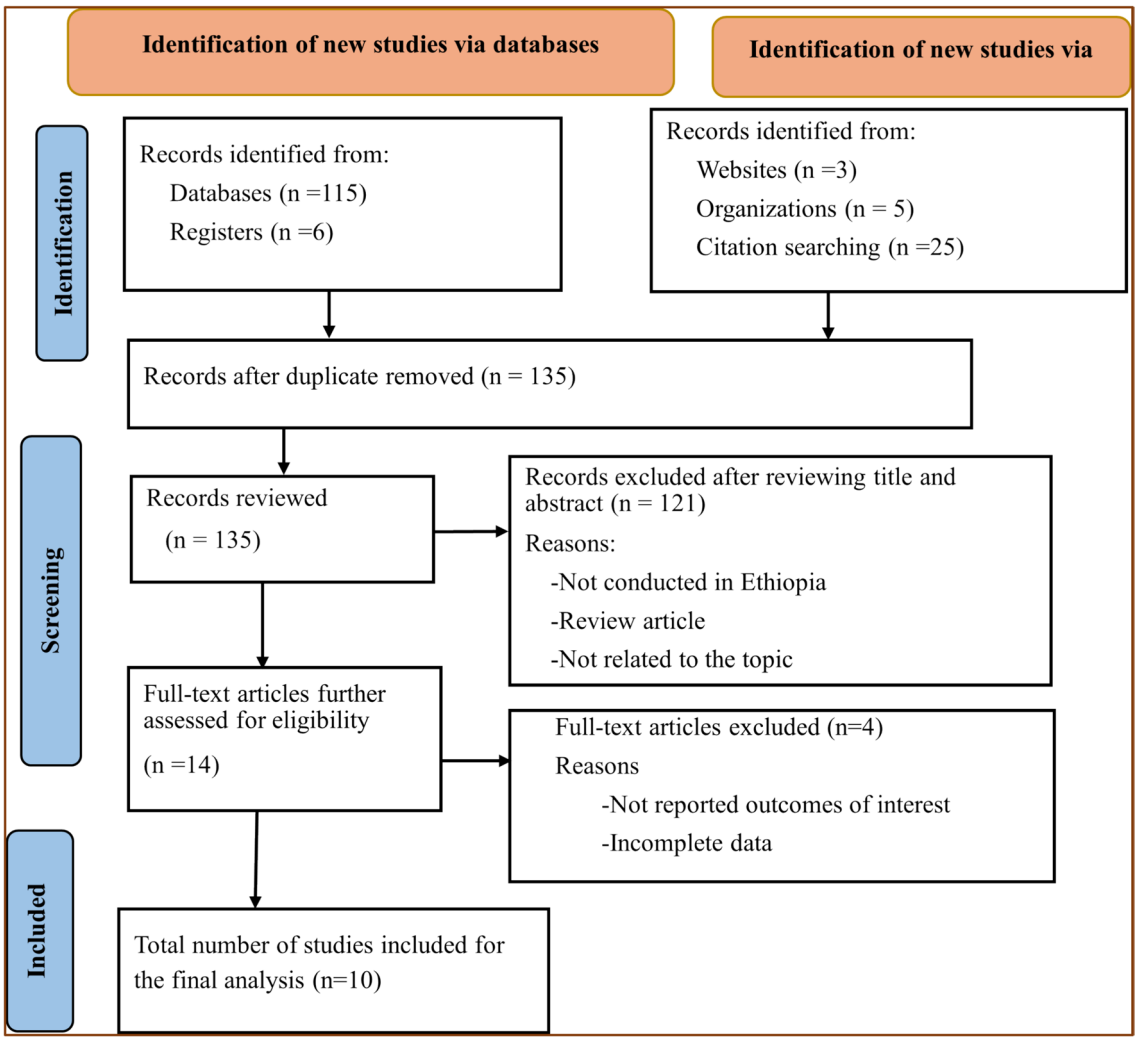

Fig. 1 PRISMA flow diagram illustrating the process of selecting eligible studies for the pooled prevalence of thrombocytopenia among malaria patients in Ethiopia

thrombocytopenia among malaria patients in Ethiopia was 70% (95% CI 63%, 77%). However, a high level of statistical heterogeneity was observed among the studies ($I^2 = 87.65\%$, Q test statistic = 68.13; $p < 0.001$), indicating significant differences in the estimates of thrombocytopenia prevalence (Fig. 2). The graphical assessment of heterogeneity using Galbraith also revealed there are 5 (out of 10) studies that are outside of the confidence bound regions, that indicating clear evidence for the presence of heterogeneity across the studies report (Fig. 3). In the absence of substantial heterogeneity, all the studies should lie within the 95% CI region (shaded area).

Handling heterogeneity

Significant heterogeneity was observed from the pooled estimate of the random model. To investigate the potential sources of this heterogeneity, sub-group analysis, sensitivity analysis, and meta-regression were carried out.

Subgroup analysis

The subgroup analysis was performed based on factors such as the geographic region where the studies were conducted, and the year the studies were published. However, the source of heterogeneity was not handled. When looking at the results by region: The highest pooled prevalence of thrombocytopenia was observed in the SNNP region (78.34%; 95% CI 66.29%, 90.39%) followed by the Amhara region (69.7%; 95%CI 55.2%, 84.2%), whereas the lowest prevalence was observed in the Gambella Region (63.4%; 95%CI (54.6%, 72.2%)). There was high heterogeneity observed in the studies from the Amhara, Oromia, and SNNP regions. The results were also examined

Table 1 Characteristics of the studies included in the pooled analysis of thrombocytopenia prevalence among malaria patients in Ethiopia

First Author	Publication Year	Region	Place	Study Design	Plasmodium species	Participants	Total Malaria patients	Thrombocytopenic cases	Thrombocytopenia-prevalence
Asmerom et.al [40]	2023	Harari	Harar	Facility based CS	Pf, Pv	Adults infected with malaria	254	172	67.72
Asmerom, H. et.al. [41]	2019	Amhara	Alamata	Facility based CS	Pf, Pv, mixed	Adults positive for malaria	119	67	56.30
Awoke, N. and Arota, A [20]	2019	SNNP	Tercha	Facility based CS	Pf, Pv	Adults positive for malaria	170	143	84.12
Mikre, K. et al. [21]	2016	SNNP	Arba Minch	Facility based CS	Pf, Pv	Adults positive for malaria	117	84	71.79
Abebe, Wagaw, et al. [42]	2024	Amhara	Dembiya	Facility based CS		Adults positive for malaria	35	21	60.00
Kassa, D. et.al. [43],	2005	Oromia	Wonji	Facility based CS	Pf, Pv	Adults positive for malaria	158	129	81.65
Gebreweld, A. et al. [5]	2021	Amhara	Ataye	Facility based CS	Pf, Pv	Adults positive for malaria	73	58	79.45
Kidu, H. G [44]	2017	Gambella	Gambella	Facility based CS	Pf	Male adults positive for malaria	60	41	68.33
Tilahun, F. et al. [45]	2021	Oromia	Adama	Facility based CS	Pf, Pv, mixed	Adults positive for malaria	101	52	51.49
Sahle, T.et al.[46]	2017	Gambella	Gambella	Facility based CS	pf, pv, mixed	Malaria-infected adults living with HIV	85	51	59.0

CS Cross-sectional study design

by year of publication: Studies published before 2016 had the highest pooled prevalence of thrombocytopenia at 77.12% (95% CI 67.50%, 86.74%). This earlier group of studies also had insignificant levels of heterogeneity (Table 2).

Sensitivity analysis

A leave-one-out sensitivity analysis was conducted to evaluate whether the exclusion of any single study altered the statistical result of the pooled prevalence of thrombocytopenia among malaria patients. This analysis involved sequentially omitting each study and recalculating the overall pooled effect size. The results demonstrated that the pooled effect size remained within the 95% CI of the overall pooled prevalence when any single study was excluded. This finding suggests it was robust, and no single study excessively influenced the overall pooled prevalence of thrombocytopenia among malaria patients in Ethiopia. The pooled estimated prevalence ranged from 67.9% (95% CI 61.0%, 74. 8%) to 71.8% (95% CI 65.3%, 78.3%) after the deletion of a single study (Table 3 and Supplementary file 4).

Meta-regression

A meta-regression analysis was also conducted to explore potential sources of heterogeneity among the studies included in the meta-analysis. It incorporated study characteristics, such as publication year and sample size as covariates in the meta-regression model. The meta-regression analysis revealed that the sample size was the variable responsible for the observed heterogeneity among the studies, as indicated by the statistically significant result ($p=0.002$) (Table 4).

Publication bias

Publication bias was examined by observation using funnel plots and shows substantial symmetry, suggesting the absence of a small study effect (Fig. 4). It was

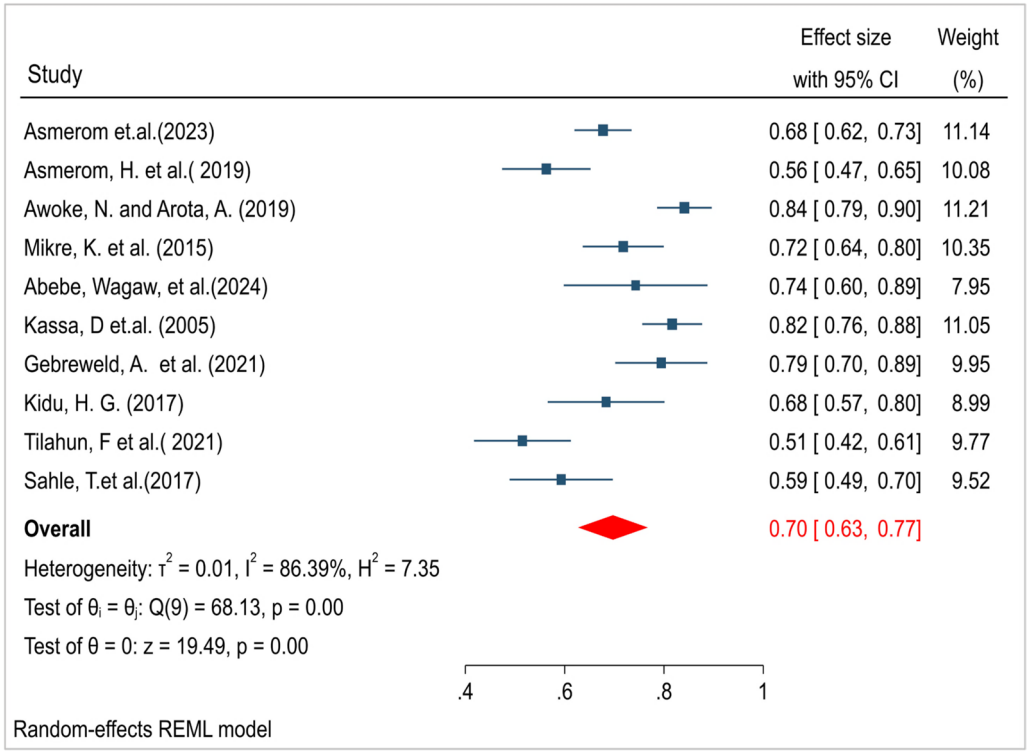

Fig. 2 Forest plot showing the pooled prevalence of thrombocytopenia among malaria patients in Ethiopia from random-effect model analysis

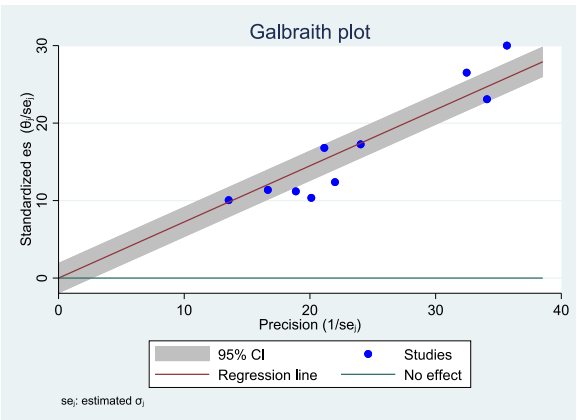

Fig. 3 Galbraith plot for heterogeneity assessment of the included studies

also statistically checked by Egger's tests and the result indicated that there was no evidence of publication bias, with a p-value of 0.137. This suggests that the included studies in the systematic review and meta-analysis were not significantly influenced by the selective publication of studies based on the direction or magnitude of their findings (Fig. 4 and Supplementary file 5).

Discussion

This systematic review and meta-analysis was conducted to estimate the overall pooled prevalence of thrombocytopenia among malaria patients in Ethiopia. Ten articles that fulfilled the eligibility criteria were included and enrolled for the final analysis. Accordingly, the overall pooled prevalence of thrombocytopenia among malaria patients in Ethiopia was found to be 70% (95% CI 62,77), with significant heterogeneity. The finding indicates a significant burden of this haematological problem among malaria patients in the country. It emphasizes how crucial it is to integrate thrombocytopenia screening in standard diagnostic malaria and management procedures to improve patients' outcomes. The significant heterogeneity observed across studies suggests that the prevalence of thrombocytopenia varies considerably depending on regional and methodological factors, warranting further investigations.

The result of this study aligns with the findings of several other large primary studies that have also reported a substantial burden of thrombocytopenia associated with malaria infection. A study conducted in Indonesia reported the prevalence of thrombocytopenia to be 87% [27]. Similarly, a study in Thailand reported a thrombocytopenia prevalence of 84.9% among patients with malaria, [28]. The consistency in the high prevalence of

Table 2 Subgroup analysis of thrombocytopenia by region, publication year, and setting

Subgroups	Category	No of studies	Pooled prevalence of thrombocytopenia (95% CI)	Heterogeneity Statistics	
				I^2 (in %)	p-value
Region	Amhara	3	69.70% (55.2, 84.2%)	82.20	0.001
	Oromia	2	66.82% (37.27, 96.37%)	96.2	< 0.001
	SNNP	2	78.34% (66.29, 90.39%)	83.4	0.014
	Gambella	2	63.40% (54.6, 72.2%)	21.37	0.259
	Harari	1	67.70% (62.0, 73.5%)	–	
Publication Year	≤2016	2	77.12% (67.50, 86.74%)	72.4	0.057
	[2017–2020]	4	69.85% (51.35, 88.35%)	93.0	< 0.001
	≥2021	4	65.14% (53.80, 76.49%)	82.8	0.001

Table 3 Result of the sensitivity analysis of the included studies for the pooled prevalence of thrombocytopenia among malaria patients in Ethiopia

Study Omitted	Prevalence (%)	95% CI (%)
Asmerom et.al, [40]	69.9%	62.0, 77. 8
Asmerom, H. et al. [41]	71.3%	64.2, 78.4
Awoke, N. and Arota, A. [20]	67.9%	61.0, 74. 8
Mikre, K. et al. [21]	69.4%	61.6, 77.3
Abebe, Wagaw. et al. [42]	69.3%	61.7, 76.9
Kassa, D. et.al. [43]	68.3%	61.0, 75.5
Gebreweld, A. et al. [5]	68.6%	61.1, 76.1
Kidu, H. G. [44]	69.8%	62.1, 77.6
Tilahun, F. et al. [45]	71.8%	65.3, 78.3
Sahle, T.et al. [46]	70.8%	63.4, 78.2
Combined	70.0%	63.0, 77.0

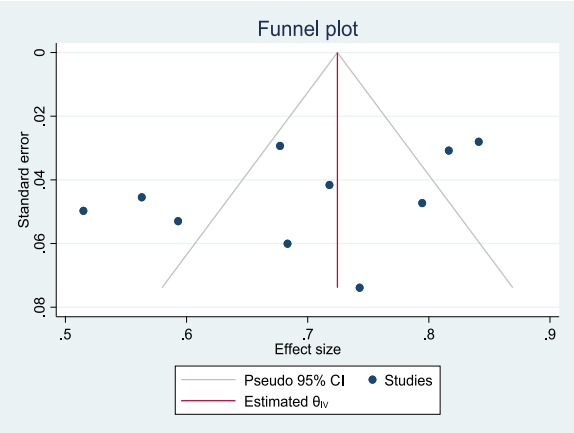

Fig. 4 Funnel plot on the prevalence of thrombocytopenia among malaria patients in Ethiopia illustrating the presence of publication bias

Table 4 Meta-regression analysis result of for the prevalence of thrombocytopenia among malaria patients in Ethiopia

Moderator	Coefficient	SE	p-value	[95% CI]	
Publication Year	0.0002	0.0024	0.921	−0.0061	0.0067
Sample Size	−0.0047	0.0007	0.002	−0.0068	−0.0026

SE Standard Error, *CI*: Confidence Interval

thrombocytopenia across these studies, conducted in different settings, underscores the strong association between malaria infection and a reduction in platelet count.

However, a lower rate of thrombocytopenia was reported in a previous meta-analysis study, which found an overall pooled prevalence of 18.7% [13]. This discrepancy is likely due to differences in the study populations, i.e. the previous meta-analysis focused specifically on patients with *P. vivax* malaria, whereas the current study assessed the pooled prevalence among all malaria patients, regardless of the species. Another meta-analysis study also reported a pooled prevalence of 21% for profound thrombocytopenia in patients with severe *P. vivax* malaria [29]. However, the findings of this study reflect the pooled prevalence of any form of thrombocytopenia, irrespective of severity or the *Plasmodium* species responsible for malaria.

The pathogenic mechanism underlying the low platelet count in malaria patients is not clear. However, previous studies highlighted that the substantial burden of thrombocytopenia associated with malaria infection can be partly due to the immune-mediated destruction of platelets [30]. In addition to direct platelet destruction, the sequestration or trapping of platelets in the spleen and other organs can also contribute to the development of thrombocytopenia [31]. The sequestration process, driven by the cytoadherence of infected red blood cells and the host's immune response, further restricts the availability of circulating platelets. Malaria infection can also cause dysmegakaryocytopoiesis, a process where the release

of inflammatory cytokines and parasite effects suppress platelet production, reducing the platelet pool's replenishment [32]. Platelets also play a crucial role in innate protection, killing *P. falciparum* and intraerythrocytic malarial parasites, resulting in a reduction of platelet count [33], leading to thrombocytopenia in the process. Furthermore, bone marrow suppression and oxidative stress are the responsible mechanisms for thrombocytopenia [32, 34]. In truth, thrombocytopenia in malaria is a multifactorial disorder, resulting from an interaction of several mechanisms rather than a single cause [35].

In this study, the subgroup analysis revealed notable regional variations in the prevalence of thrombocytopenia. The highest prevalence was observed in the Southern Nations, Nationalities, and Peoples' (SNNP) region (78.34%), followed by the Amhara region (69.7%). In contrast, the Gambella region reported the lowest prevalence at 63.4%. These differences could be attributed to regional disparities in malaria transmission, the predominant malaria species, and differences in healthcare access and diagnostic practices across regions. Understanding these regional differences is crucial for developing targeted interventions and improving the management of thrombocytopenia. Moreover, the highest prevalence in the SNNP region suggests a more severe form of malaria, which is a strong risk factor for thrombocytopenia [9]. Additionally, the regional disparities may also be due to the difference in local malaria control efforts, and environmental factors like varying climatic conditions [36, 37].

The meta-regression analysis identified sample size as a significant factor contributing to the heterogeneity among studies ($p = 0.001$), suggesting that studies with smaller sample sizes might have a biased estimate. The identification of sample size as a source of heterogeneity highlights the importance of ensuring adequate sample sizes in future studies to obtain more reliable and generalizable estimates of thrombocytopenia prevalence [38]. Larger sample sizes generally provide more precise estimates and can help reduce variability in prevalence estimates [39].

Implications for public health and clinical practice

The higher frequency of thrombocytopenia in malaria patients calls for increased caution in clinical management. Routine platelet count evaluations should be practiced in malaria patients, especially in areas where the disease is highly prevalent. Additionally, the regional differences in prevalence highlight the necessity of region-specific malaria control practice.

Limitations and future research

Despite its strength, this study is not without limitations. The significant heterogeneity observed among studies, although partially explained by sample size, may raise concerns about the generalizability of the findings. Additionally, the reliance on observational studies, which are inherently prone to biases, might have influenced the pooled prevalence estimate. Furthermore, since all the studies included in the analysis were conducted in healthcare facilities, it may lead to an overestimation of the effect size estimate and may not accurately represent the actual epidemiology of the problem. Hence, large nationwide community-based epidemiological studies should be conducted to establish the true burden of thrombocytopenia in malaria patients and to investigate its primary contributing factors. Moreover, further research is needed to explore other potential heterogeneity sources including diagnostic criteria for thrombocytopenia, *Plasmodium* species variations, and patient demographics.

Conclusion

This study provides valuable insights into the pooled prevalence of thrombocytopenia among malaria patients in Ethiopia, with an overall prevalence of 70%, indicating the substantial burden of the problem. The findings highlight the need for region-specific public health strategies and the importance of routine platelet monitoring in the clinical management of malaria. However, the study's findings should be interpreted with caution due to limitations, including reliance on observational data that might be prone to biases, and potential overestimation of prevalence due to the exclusive inclusion of healthcare facility-based studies. To address these, future large population-based studies research should be carried out to estimate the true burden of thrombocytopenia and its contributing factors. Moreover, region-specific public health strategies and routine platelet monitoring in malaria management should be implemented to mitigate the burden of thrombocytopenia and improve clinical outcomes.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12936-025-05296-8.

Supplementary material 1
Supplementary material 2
Supplementary material 3
Supplementary material 4
Supplementary material 5

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Author contributions
All authors contributed to the conception, design, and execution of this study. A.B.K and M.S.A conducted the literature search and data extraction. K.T.T, A.D and A.B.K performed the statistical analysis. A.G, H.G, and M.S.A did the drafted sections of the manuscript and prepared the panel and figure of the manuscript. The final manuscript was approved by all authors after a critical review.

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Availability of data and materials
The corresponding author can provide the datasets generated and analysed during the current investigation upon reasonable request.

Declarations

Ethics approval and consent to participate
Since this was a systematic review and meta-analysis of previously published research, no participant consent nor ethical clearance was needed.

Competing interests
The authors declare no competing interests.

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