The prevalence of thrombocytopenia among pregnant women in Ethiopia: a systematic review and meta-analysis

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Abstract

Background Throughout pregnancy, haematopoietic changes, including notable variations in blood volume, occur to meet the demands of the developing fetus and placenta. Thrombocytopenia is a typical hematological disorder during pregnancy, next to anemia. Extreme thrombocytopenia during pregnancy may increase the risk of heavy bleeding during or after delivery. Findings on the prevalence of thrombocytopenia among pregnant women varied in Ethiopia. Therefore, this review aimed to determine the pooled prevalence of thrombocytopenia among pregnant women in Ethiopia.

Methods The databases (PubMed, Scopus, Hinari, Cochrane Library, and Google Scholar) were searched for relevant studies using MeSH Terms and keywords related to thrombocytopenia. The systematic review and meta-analysis were carried out following PRISMA guidelines. Data analysis was conducted using R statistical software version 3.6.1. A random-effect model was fitted to estimate the pooled prevalence of thrombocytopenia among pregnant women. The heterogeneity of included studies was examined using I^2 test statistics. Egger weighted regression analysis and funnel plots were employed to detect publication bias.

Results Six of the 29 studies retrieved were eligible for this systematic review and meta-analysis. The pooled prevalence of thrombocytopenia among pregnant women in Ethiopia was 10.7% (95% CI: 8.6, 13.0%). Its severity was found to be 8.3% ($I2=24\%$) mild, 1.7% ($I2=0\%$) moderate, and 0.6% ($I2=29\%$) severe. The highest prevalence of thrombocytopenia was observed in the SNNPR at 14.1% (95% CI: 11.5, 17.0%), whereas the lowest prevalence was in Addis Ababa at 7.7% (95% CI: 8.6, 6.34%).

Conclusion The pooled prevalence of thrombocytopenia among Ethiopian pregnant women in this research was remarkable, indicating the necessity to screen pregnant women for possible thrombocytopenia and provide them with the necessary treatments.

Keywords Prevalence, Thrombocytopenia, Pregnancy, Women, Ethiopia

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Introduction

Hematological changes, including significant changes in blood volume, take place throughout pregnancy to meet the needs of the growing fetus and placenta. The direct effects of progesterone and estrogen on the kidney, which result in the release of renin and the activation of the aldosterone renin-angiotensin system, cause an average rise in plasma volume of 40 to 45%. As a result, there is an increase in body water overall and renal sodium retention. However, due to hemodilution, increased platelet activation, and consumption, especially in the third trimester, the platelet count drops during pregnancy [1–3]. According to studies, pregnant women are four times more likely than non-pregnant women to have low platelet count [4].

Thrombocytopenia is a disorder characterized by a decreased platelet count. Between 6 and 15% of pregnancies are affected by it, which is the second most common cause of hematological abnormalities during pregnancy next to anemia [5, 6]. Human platelet counts typically range from 150,000 to 450,000/ mm^3. Platelet counts below 150,000 cells/mcL are considered to be indicative of thrombocytopenia, which can be mild (100,000–150,000/ mm^3), moderate (50,000–100,000/ mm^3), or severe (less than 50,000/mm^3) [7].

Most low platelet counts during pregnancy are brought on by gestational thrombocytopenia (GT), idiopathic thrombocytopenic purpura (ITP), or preeclampsia [8]. Other causes include illnesses such as leukemia and aplastic anemia as well as infections such as malaria or a folate deficiency [9].

Pregnant women with thrombocytopenia are more likely to experience excessive bleeding during or after delivery, especially if they require a cesarean section or other type of medical procedure during pregnancy or labor. When the platelet count is less than 50,000/mm^3, such bleeding issues are more prone to occur [10].

Pregnancy-related thrombocytopenia has led to needless, frequently invasive extra tests and cesarean deliveries. The diagnosis and care for this ailment can be costly, upsetting for the patient, and have unfavorable effects. Pregnancy-related thrombocytopenia is poorly recognized and treated. Although it has been discussed in numerous types of research, it is crucial to conduct a more thorough analysis, such as a meta-analysis, to clarify the pooled prevalence and variability between various samples due to the variety of the numbers discovered in different studies. Therefore, this systematic review and meta-analysis aimed to estimate the pooled prevalence of thrombocytopenia among pregnant women in Ethiopia.

Methods

Study protocol and reporting

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines for literature search strategy, selection of studies, data extraction, and result reporting were followed while conducting this systematic review and meta-analysis [11]. The protocol has been registered in PROSPERO, an International Prospective Register of Systematic Reviews, with the registration number CRD42022338163.

Eligibility criteria

This review included studies based on the Condition, Context, and Population (**CoCoPo**) principle, adapted from the JBI 2017 review guideline [12], conducted and published in a peer-reviewed journal, with participants residing in Ethiopia. Cross-sectional studies that reported the outcome of interest and published articles in the English language were eligible for inclusion. Case reports, case reviews, and studies conducted among pregnant women who had comorbidities like HIV/AIDS and hypertension were excluded from the study. In addition, studies with poor methodological quality were excluded. There was no time restriction for the articles published to pool the prevalence of thrombocytopenia.

Types of population pregnant women who reported having thrombocytopenia.

Context Every cross-sectional study was done on the prevalence of thrombocytopenia among pregnant women in different parts of Ethiopia.

Condition This review considered the studies that measured the outcome of the interest-based prevalence of thrombocytopenia.

Variable and measurement

The primary outcome of this study was thrombocytopenia. The case definition of thrombocytopenia was a platelet count of less than 150,000 per mm^3. Thrombocytopenia can be classified as mild (platelet count of 100,000 – 150,000 per mm^3), moderate (platelet count of 50,000 – 100,000 per mm^3, or severe (platelet count of less than 50,000 per mm^3).

Information sources and search strategies

Databases PubMed, Scopus, Hinari for health via Research4Life, Cochrane Library, and Google Scholar were accessed. Further searches were made through snowballing or retrieving relevant references used in related studies. A combination of medical subject headings (MeSH terms) using Boolean operators and keywords related to thrombocytopenia were used to search

the studies. The last date to access databases was made on May 13, 2023, on Friday at 4:40 PM.

Study selection

Endnote (version X9) reference management software was used to download, organize, review, and cite related articles. Duplicate studies were removed using Endnote and manually. The relevance of the studies was screened by two independent reviewers (Belayneh Hamdela (BH) and Mesfin Menza (MM)). During the preliminary assessment, after reading the title and abstract, primary studies found to be irrelevant were excluded. When discrepancies between two reviewers happened, the third independent reviewer (Solomon Gebre) was used to handle the discrepancy based on its relevance to pre-specified objectives and inclusion criteria. The primary studies with only relevant information that fulfilled inclusion criteria were selected for full-text review, and reasons for exclusion were presented using the PRISMA flow diagram.

Risk of bias assessment

Two independent reviewers (BH and MM) appraised the methodological quality of each study using the 2017 JBI Critical Appraisal Checklist for prevalence studies [12]. The discrepancy was solved by a discussion with the third independent reviewer (SG). After evaluation of each study against these criteria, only studies with a minimum score of 50% and above were included.

Data extraction

Studies that fulfilled the eligibility criteria were subjected to data extraction by two reviewers (BH and MM) independently and summarized into an Excel spreadsheet. Disagreements were resolved through consensus and discussion with a third reviewer (SG). The following items were extracted for analysis: author name, year of publication, sample size, total number of cases, study design, thrombocytopenia prevalence with its severity level, and the region where the study was conducted. The extracted data was then edited and saved in a comma-delimited (CSV) file format to suit the analysis.

Statistical analysis

The data extracted and saved in CSV format in an Excel spreadsheet were imported into R version 3.6.1 statistical software for the analysis. Before pooling the effect sizes, the summary measures were transformed into suitable transformations that result in a normal distribution. Accordingly, the proportion of thrombocytopenia was transformed into the Freeman and Tukey double arcsine transformation (PFT). When the observed proportions of each study are either below 0.20 or above 0.80, double arcsine transformation is advisable [13]. In these

circumstances, the log transformation can be limited in its ability to stabilize the variance. To overcome this constraint of the log transformation or to stabilize the variance, the PFT is the alternative option, and it provides a more accurate estimate of the weighted average. All analysis was done using transformed summary measures. For reporting, back translation of the summary measures was done because it made the results easier to interpret for readers. The heterogeneity of the studies was examined using two methods: first, a forest plot (subjective method) was used to assess graphically, and second, using the I-squared statistic (objective method), which indicated that 25, 50, and 75%, represented low, moderate, and high heterogeneity, respectively [14]. In a random effects model, the pooled effect size (prevalence of thrombocytopenia) was estimated using Dar-Simonian Liard (DL). To measure the degree of heterogeneity in the random effect model, tau squared was used. The subgroup analysis was conducted to deal with heterogeneity. Accordingly, the subgroup analysis was carried out for the regions, which was further used to report the regional pooled prevalence of thrombocytopenia. Potential publication bias was examined using a funnel plot subjectively and Egger's regression test objectively. In Egger's test, a $P < 0.05$ was considered a statistically significant publication bias [15].

Results

Search results

Initially, a total of 22 studies were retrieved from the electronic databases and 7 articles were retrieved through manual searching. From this, 12 duplicates were found and removed. The remaining 17 articles were screened by their title and abstract and 9 irrelevant studies were removed. Eight full-text articles were assessed for eligibility and 2 of them were excluded due to poor methodological quality. Finally, a total of 6 studies fulfilled the inclusion criteria and enrolled in the study (Fig. 1).

Study characteristics

All included studies were health facility-based cross-sectional studies. The studies were conducted between 2015 and 2021. The participants included in those primary studies were pregnant women. Thrombocytopenia among all study participants in all primary studies was diagnosed based on a platelet count of less than 150,000 per mm^3.

In this review, a total of six articles from Ethiopia were included, which consists of 1,694 study participants. Out of 1,694 study participants, 186 had thrombocytopenia. The sample size across the studies ranges from 193 in Hawassa University Teaching and Referral Hospital [16] to 422 in Wolkite University Teaching and Referral Hospital [17]. Out of the six articles, three were conducted in
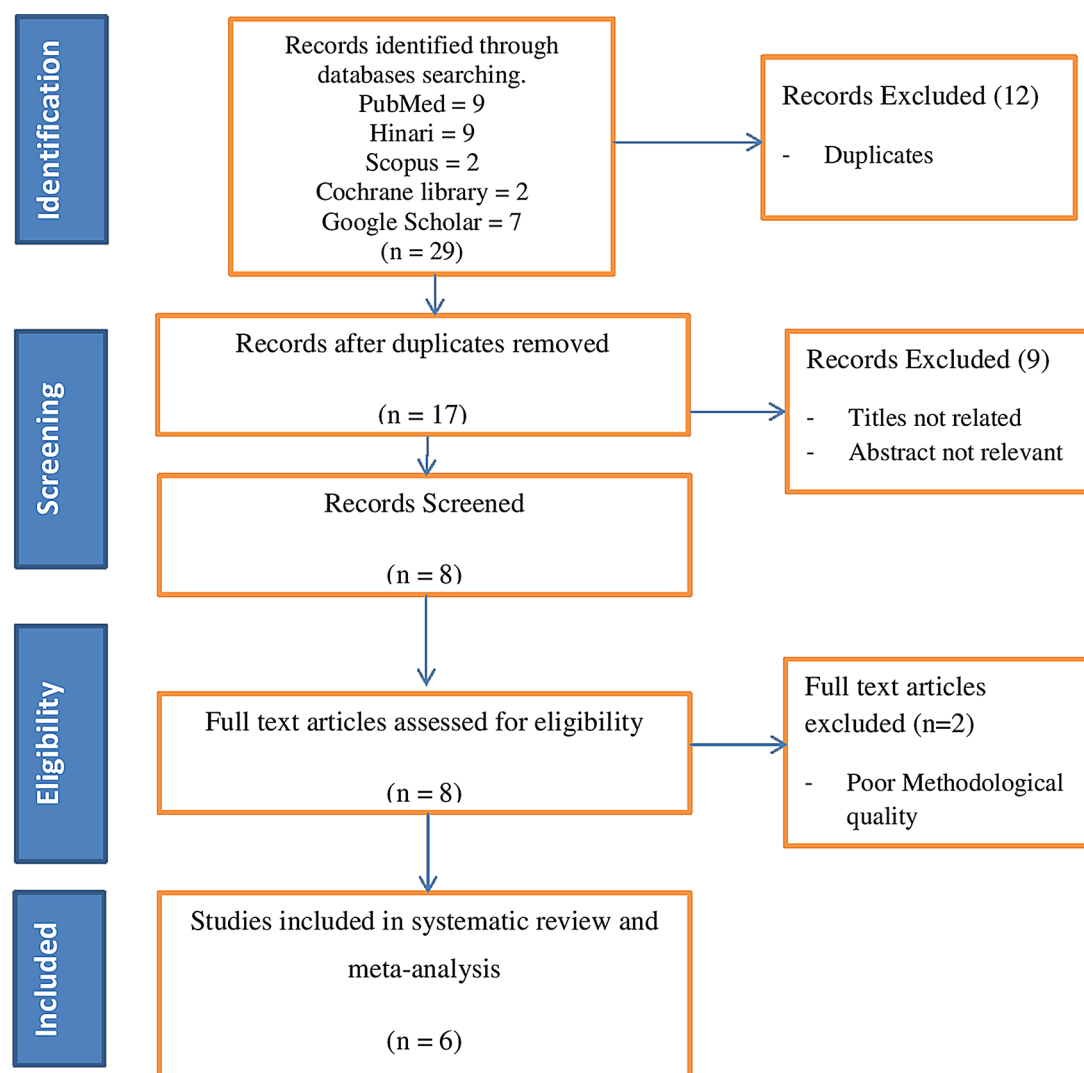
Fig. 1 Study selection procedure for the systematic review and meta-analysis, Ethiopia

the Amhara region [18–20], one in Addis Ababa [21], and two in the Southern Nations, Nationalities and People Region (SNNPR) [16, 17]. All the primary studies were conducted to determine the prevalence of thrombocytopenia among pregnant women. In those primary studies, the minimum prevalence of thrombocytopenia was 7.7%, which was from St. Paul's Hospital [21], and the maximum prevalence of thrombocytopenia was observed in Wolkite University Specialized Hospital, 14.5% [17]. All of the studies reported the severity level of thrombocytopenia as mild, moderate, or severe. In those primary studies, the highest prevalence was for mild thrombocytopenia, which is lower in Dessie Comprehensive Specialized Hospital, 72.4%, and higher in St. Paulos Hospital, 90.1% from thrombocytopenic mothers. Regarding severe forms of thrombocytopenia, the highest prevalence was observed in Hawassa University Teaching and Referral Hospital, 11.5%. Moreover, the characteristics of the studies included in the meta-analysis are described in (Table 1).
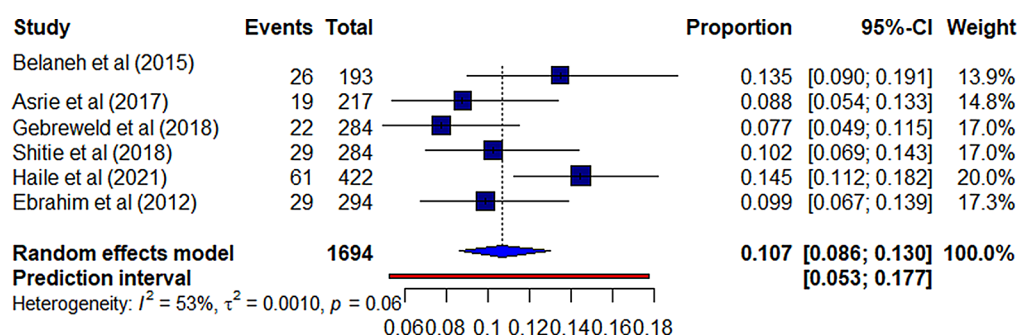
Prevalence of thrombocytopenia

In the fixed effect model, the pooled effect size of thrombocytopenia showed a moderate heterogeneity ($I^2 = 53\%$, $P < 0.001$). Therefore, the random effect model was chosen to determine the pooled prevalence of thrombocytopenia. In the random effect model, using a Drasimonoial laird (DL) and PFT, the pooled prevalence of thrombocytopenia in Ethiopia was 10.7% (95% CI: 8.6, 13%) (Fig. 2).

Additionally, in the random effect model, the pooled prevalence based on the severity level of thrombocytopenia has shown that 8.3% ($I^2 = 24\%$) mild, 1.7% ($I^2 = 0\%$) moderate, and 0.6% ($I^2 = 29\%$) severe thrombocytopenia (S1 Fig) and summarize under (Table 2).

Table 1 Characteristics of primary studies included in the systematic review and meta-analysis, Ethiopia, 2023

Author (Year)	Region	Setting	Study Participant	Study Design	Sample	Cases	Prevalence	Mild	Moderate	Severe
Asrie et al. (2017)	Amhara	Gondar University Hospital	Pregnant Women	Cross-sectional	217	19	0.088	0.74	0.157	0.103
Haile et al. (2021)	SNNPR	Wolkite University Specialized Hospital	Pregnant Women	Cross-sectional	422	61	0.145	0.77	0.164	0.066
Gebreweld et al. (2018)	Addis Ababa	St. Paul's Hospital	Pregnant Women	Cross-sectional	284	22	0.077	0.901	0.091	0
Shitie et al. (2018)	Amhara	Debre Berhan Referral Hospital	Pregnant Women	Cross-sectional	284	29	0.102	0.758	0.206	0.0345
Ebrahim et al. (2021)	Amhara	Dessie Comprehensive Specialized Hospital	Pregnant Women	Cross-sectional	294	29	0.099	0.724	0.172	0.104
Belaneh et al. (2015)	SNNPR	Hawassa University Teaching and Referral Hospital	Pregnant Women	Cross-sectional	193	26	0.135	0.731	0.153	0.115

Study	Events	Total	Proportion	95%-CI	Weight
Belaneh et al (2015)	26	193	0.135	[0.090; 0.191]	13.9%
Asrie et al (2017)	19	217	0.088	[0.054; 0.133]	14.8%
Gebreweld et al (2018)	22	284	0.077	[0.049; 0.115]	17.0%
Shitie et al (2018)	29	284	0.102	[0.069; 0.143]	17.0%
Haile et al (2021)	61	422	0.145	[0.112; 0.182]	20.0%
Ebrahim et al (2012)	29	294	0.099	[0.067; 0.139]	17.3%
Random effects model		**1694**	**0.107**	**[0.086; 0.130]**	**100.0%**
Prediction interval				**[0.053; 0.177]**	

Heterogeneity: $I^2 = 53\%$, $\tau^2 = 0.0010$, $p = 0.06$

0.06 0.08 0.1 0.12 0.14 0.16 0.18

Fig. 2 Forest plot showing heterogeneity among included studies to estimate the prevalence of thrombocytopenia, Ethiopia, 2023

Table 2 Key findings of the review

Variables	Pooled prevalence (%)	95% CI
Thrombocytopenia	10.7	8.6, 13
Mild thrombocytopenia	8.3	6.8, 9.9
Moderate thrombocytopenia	1.7	1.1, 2.4
Severe thrombocytopenia	0.6	0.2, 1.2

Subgroup analysis

The heterogeneity that was observed in a fixed effect model disappeared when subgroup analysis was done for the region ($P > 0.05$). The subgroup analysis based on region showed that the highest prevalence of thrombocytopenia was observed in the SNNPR at 14.1% (95%CI: 11.5, 17%) whereas the lowest prevalence was in Addis Ababa at 7.7% (95%CI: 8.6, 6.34%) (Fig. 3).

Publication bias

Potential publication bias was assessed visually by funnel plot. The funnel plot of the included studies is symmetrical and it seems that there is no publication bias to fit the trim and fill analysis. Besides, Egger's test indicated that there is no publication bias ($P = 0.4384$ (Fig. 4).

Discussion

This review was conducted to determine the pooled prevalence of thrombocytopenia among pregnant women in Ethiopia. Accordingly, the pooled prevalence of thrombocytopenia was 10.7% (95% CI: 8.6, 13). The pooled prevalence of mild thrombocytopenia was 8.3%, the pooled prevalence of moderate thrombocytopenia was 1.7% and the pooled prevalence of severe thrombocytopenia was 0.6% among thrombocytopenic pregnant women in Ethiopia.

In this review, the pooled prevalence of thrombocytopenia among pregnant women was remarkable. The result indicates that a sizeable proportion of pregnant women are being affected by the hematological disorder that needs early detection and treatment of thrombocytopenia during pregnancy. The result was comparable to the systematic review and meta-analysis conducted in Africa in 2022, which was 10.23% [22]. However, the finding of this review was higher than the systematic review and meta-analysis conducted globally in 2019, which was 8.4% [23]. The variations in the estimates might be due to differences in study design, study setting, sample size, and other population characteristics. Additionally, changes in nutritional status and the frequency of intestinal parasitic
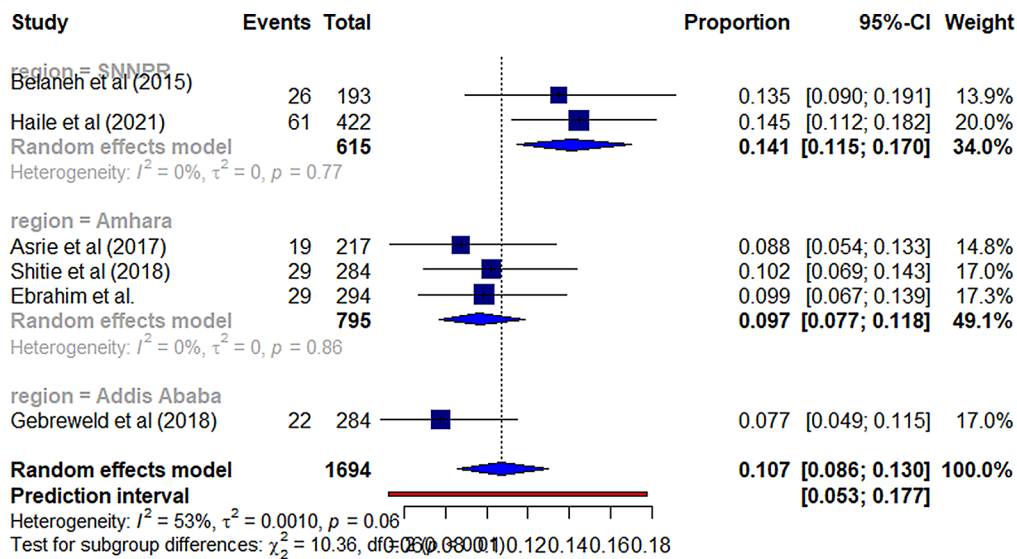
Fig. 3 Forest plot showing sub-group analysis among included studies to estimate the prevalence of thrombocytopenia, Ethiopia, 2023
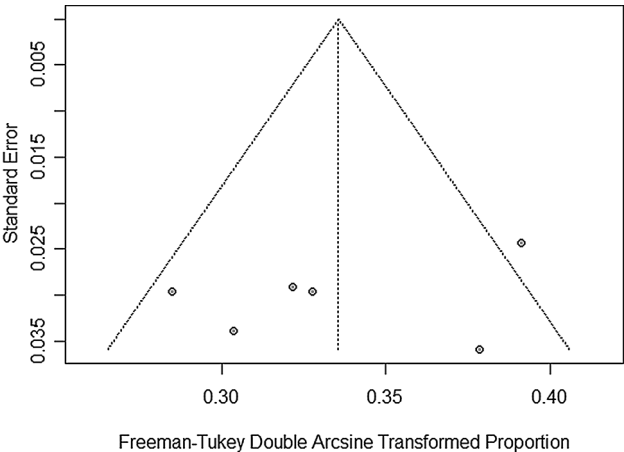

Fig. 4 Funnel plot showing publication bias for the prevalence of thrombocytopenia, Ethiopia, 2023

infections during pregnancy might be associated with the rise in thrombocytopenia in different settings.

The results of the subgroup analysis by Region revealed that Addis Ababa had the lowest prevalence of thrombocytopenia, 7.7%, and the SNNPR had the highest prevalence, 14.1%. This shows that there is variation in the prevalence of thrombocytopenia across the regions. This difference might be due to variations in progressive improvement in the health care services such as prenatal care, and nutritional status of pregnant women across the regions. Also, variations in sample size, eligibility criteria, and population characteristics across the regions could be a possible explanation. Furthermore, in the included studies in this review, pregnant women might have experienced thrombocytopenia due to a variety of conditions, including anemia, preeclampsia, hypertensive diseases, malaria, and undiagnosed HIV infection which might

have increased the prevalence and contributed to the variations.

According to severity levels, mild type thrombocytopenia was the predominant type which affected 8.3% of pregnant women followed by moderate thrombocytopenia, 1.7%, and severe thrombocytopenia, 0.6%. The result indicates that the mild type of thrombocytopenia was more common than the moderate and severe ones. This further indicates that there is a high potential for mild cases to be progressed to severe form unless appropriate screening and early treatments are given. Further meta-analysis to compare and discuss the pooled prevalence of thrombocytopenia based on the severity levels should be considered.

Despite the efforts made to manage, this review might have limitations. This review considered only six publications from three regions of Ethiopia and some other sources might not be accessed. As a result, the pooled prevalence of thrombocytopenia may have lacked national representativeness.

Supplementary Information

Supplementary Material 1

Supplementary Material 2

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Declarations

Ethical approval
Not applicable.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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