

Review Article

The Global Prevalence of Thrombocytopenia among Pregnant Women: A Systematic Review and Meta-Analysis

Mohammad Mohseni, Zoleykha Asgarlou¹, Saber Azami-Aghdash², Sepideh Gareh Sheyklo³, Nikta Tavananezhad⁴, Ahmad Moosavi⁵

Health Management and Economics Research Center, Iran University of Medical Sciences, Tehran, ¹Department of Midwifery, School of Nursing and Midwifery, Zanjan University of Medical Sciences, Zanjan, ²Tabriz Health Services Management Research Center, Health Management and Safety Promotion Research Institute, Tabriz University of Medical Sciences, Tabriz, Departments of ³Obstetrics and Gynecology and ⁵Health and Community Medicine, Dezfoul University of Medical Sciences, Dezfoul, ⁴Department of Midwifery, Faculty of Nursing and Midwifery, Islamic Azad University, Sanandaj, Iran

ORCID:

Mohammad Mohseni: <http://orcid.org/0000-0003-1747-6542>;
Zoleykha Asgarlou: <https://orcid.org/0000-0002-3895-0517>;
Saber Azami-Aghdash: <http://orcid.org/0000-0003-1244-359X>;
Sepideh Gareh Sheyklo: <https://orcid.org/0000-0003-4375-0234>;
Nikta Tavananezhad: <https://orcid.org/0000-0001-6923-1243>;
Ahmad Moosavi: <https://orcid.org/0000-0003-1134-1022>

ABSTRACT

Background: Thrombocytopenia (TCP) is a common disorder during pregnancy. Its prevalence among pregnant women is four times greater than nonpregnant women. **Objectives:** This study aimed at determining the global prevalence of TCP among pregnant women. **Methods:** This systematic review and meta-analysis was conducted in 2018. The PubMed, Scopus, Google Scholar, Magiran, and IranMedex databases were searched using the following key words: “TCP,” “pregnancy,” “pregnant,” “pregnant women,” “gestational,” and “platelets.” The titles and the abstracts of the retrieved studies were screened to identify potentially relevant studies. Articles were included if they were the reports of original researches, included data on the prevalence of TCP among pregnant women, were in English or Persian, and had been published from January 1, 2000 to September 1, 2018. Eligible studies were appraised using the Strengthening the Reporting of Observational Studies in Epidemiology checklist. Finally, a data collection form was used to extract data. The overall prevalence of TCP among pregnant women was estimated using meta-analysis and the Comprehensive Meta-Analysis Software. Heterogeneity was evaluated through the Chi-square test and the I^2 statistic, and funnel plot was used to evaluate the possibility of publication bias. **Results:** Among 1592 studies retrieved during literature search, sixteen were included in meta-analysis. The overall prevalence of TCP among pregnant women based on the random effects model was 8.4% (95% confidence interval: 6.9%–10.1%). The lowest TCP prevalence was 4.3% in Taiwan, while the highest prevalence was 15.3% in Ghana. Gestational TCP was the most common cause of TCP among pregnant women. **Conclusion:** With a global prevalence of 8.4%, TCP in pregnancy affects around one-tenth of pregnant women in the world. Thus, timely diagnostic, preventive, and therapeutic measures are needed to effectively manage TCP in pregnancy.

KEYWORDS: Iran, Meta-analysis, Pregnancy, Prevalence, Thrombocytopenia

Address for correspondence: Dr. Ahmad Moosavi, Department of Health and Community Medicine, Dezfoul University of Medical Sciences, Dezfoul, Iran. E-mail: dr_ahmad_moosavi@yahoo.com

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INTRODUCTION

Thrombocytopenia (TCP) refers to abnormally low levels of circulating platelets.^[1] It occurs in about 6%–15% of all pregnant women. Gestational TCP, the most common cause of TCP during pregnancy, accounts for about 75% of all cases of TCP among pregnant women.^[2-4] TCP is four times more prevalent among pregnant women than nonpregnant women.^[5,6]

Platelets play significant role in hemostasis. Thus, severe TCP, i.e., a platelet count of <100,000/ μ L, can be associated with increased risk for serious bleeding^[1,3] Similarly, severe TCP in pregnancy can cause serious bleeding and subsequently maternal and fetal complications.^[7]

There are several causes for TCP in pregnancy, including gestational TCP, acute fatty liver of pregnancy, preeclampsia, and hemolysis, elevated liver enzymes, and low platelets (HELLP) syndrome.^[8,9]

Most pregnant women with TCP are healthy and asymptomatic, have no history of TCP, and are incidentally diagnosed with TCP during blood testing. This kind of TCP is called incidental or gestational TCP and usually has no significant effects on pregnancy, labor, delivery, and the newborn.^[10]

The results of previous studies into the prevalence of TCP in pregnancy do not provide a comprehensive framework for clinical decision-making because they were conducted in small populations and samples. A strategy to increase the usefulness and the applicability of the findings of these studies is to systematically analyze them.

Objectives

The present study was conducted to systematically review the previous studies into the prevalence of TCP in pregnancy and thereby, determine the global prevalence of TCP among pregnant women.

METHODS

Design

This systematic review and meta-analysis was conducted in 2018 based on the Preferred Reporting Items for Systematic Reviews and Meta-Analysis statement.^[11]

Search strategy

Data were collected through searching the existing literature. Online databases, namely PubMed, Scopus, Google Scholar, Magiran, and IranMedex were searched using the following key words: “TCP,” “pregnancy,” “pregnant,” “pregnant women,” “gestational,” and “platelets.” Boolean operators, namely “AND,” “OR,” and “NOT,” were used to narrow or broaden search

results. Search results were exported to the EndNote X5 (Thomson Reuters, New York, NY, USA) to assess the titles and the abstracts of the studies and to identify duplicate records. Moreover, the reference lists of eligible articles were also hand searched for additional studies.

Study selection and quality appraisal

Two reviewers (M.M and AM) independently screened the titles and the abstracts of the articles to identify potentially relevant studies. Then, they independently performed eligibility assessment. Any disagreement between them was resolved based on the comments of a third reviewer (S.AA). Articles were included if they were the reports of original researches, included data on the prevalence of TCP among pregnant women, were in English or Persian, and had been published from January 1, 2000 to September 1, 2018. Interventional and qualitative studies, case reports, proceedings, and studies into the prevalence of TCP among women with serious health conditions (such as acquired immunodeficiency syndrome) were not included. Two reviewers (S.G and ZA) independently appraised the retrieved studies using the Strengthening the Reporting of Observational Studies in Epidemiology checklist.^[12,13] This checklist contains 22 items. The articles that did not passed at least half of items were excluded from the study.

Data extraction

A standard data collection form was used to extract data on the following items from the retrieved articles: author, publication year, country, study design, sample size, TCP prevalence, and conclusion.

Data analysis

The overall prevalence of TCP in pregnant women was estimated by performing meta-analysis using the Comprehensive Meta-Analysis software (version 2, Biostat, Inc., Englewood, NJ, USA). Forest plots with 95% confidence interval (95% CI) were used to report the results. The heterogeneity of the studies was evaluated through the Chi-square test and the I^2 statistic ($P > 0.05$ or $I^2 > 50\%$). Publication bias was investigated visually using funnel plots^[14] and statistically using Egger's test. Graphs were drawn using the Microsoft Office Excel 2010.

RESULTS

Of 1592 studies identified in the initial search, 1205 were removed due to duplicates. Furthermore, in the title and abstract screening, 355 studies, and in the full-text screening, 16 cases were excluded. In total, sixteen studies on 36,499 pregnant women with TCP were included [Figure 1]. Studies had been conducted between

2001 and 2018 in India (five studies), Iran (three studies), Pakistan, Ethiopia, Sudan, Taiwan, Ghana, Spain, Iraq, and Cameroon (one in each country). Table 1 shows the characteristics of these sixteen studies.

The lowest TCP prevalence was 4.3% in Taiwan^[15] and 5.2% in Iran,^[16] while the highest TCP prevalence was 15.3% in Ghana^[6] and 13.4% in Sudan.^[17]

The meta-analysis of these sixteen studies showed that the overall prevalence of TCP based on the random effects model was 8.4% (95% confidence interval [CI]: 6.9%–10.1%). For TCP prevalence in each study, 95% CI was drawn in the horizontal line format [$Q = 267.9$, $df = 15$, $P < 0.05$, $I^2 = 94.4$; Figure 2]. Due to high heterogeneity of results, sensitivity analysis was done with excluding Bai *et al.*,^[18] Vyas *et al.*,^[19] Lin *et al.*,^[15] and Yazdani *et al.*^[16] The results showed that after sensitivity analysis, heterogeneity improved considerably ($Q = 31$, $df = 12$, $P < 0.05$, $I^2 = 62$). After this change, the overall prevalence of TCP based on the random effect model was 9.2%. Funnel plot was used to evaluate publication bias. Its results showed that there was a possibility of publication bias among the studies [Figure 3]. There was statistically

significant evidence of publication bias for Begg and Egger's test ($P < 0.05$). Subgroup analysis was done by country [Table 2] and showed a homogenous result in India ($Q = 1.8$, $df = 4$, $P = 0.75$, $I^2 = 0.00$).

DISCUSSION

This study aimed to determine the global prevalence of TCP among pregnant women. Findings revealed that the global prevalence of TCP in pregnancy was 8.4%, and the most common cause of TCP in pregnancy was gestational TCP. The lowest and the highest prevalence rates of TCP were 4.3% and 15.3%, respectively.^[7]

During our literature search, we found studies into the prevalence of TCP among pregnant women with serious health conditions. For instance, a study on pregnant women with acquired immunodeficiency syndrome who were not under treatment reported a TCP prevalence of 5.3%.^[20] Another study on pregnant women with hypertensive disease of pregnancy also found that 23.5% of them had TCP.^[21] Moreover, TCP prevalence among women who used cocaine was reported to be 6.7%.^[22] However, there is a paucity of studies into the effects of different health conditions on TCP. Thus, further studies,

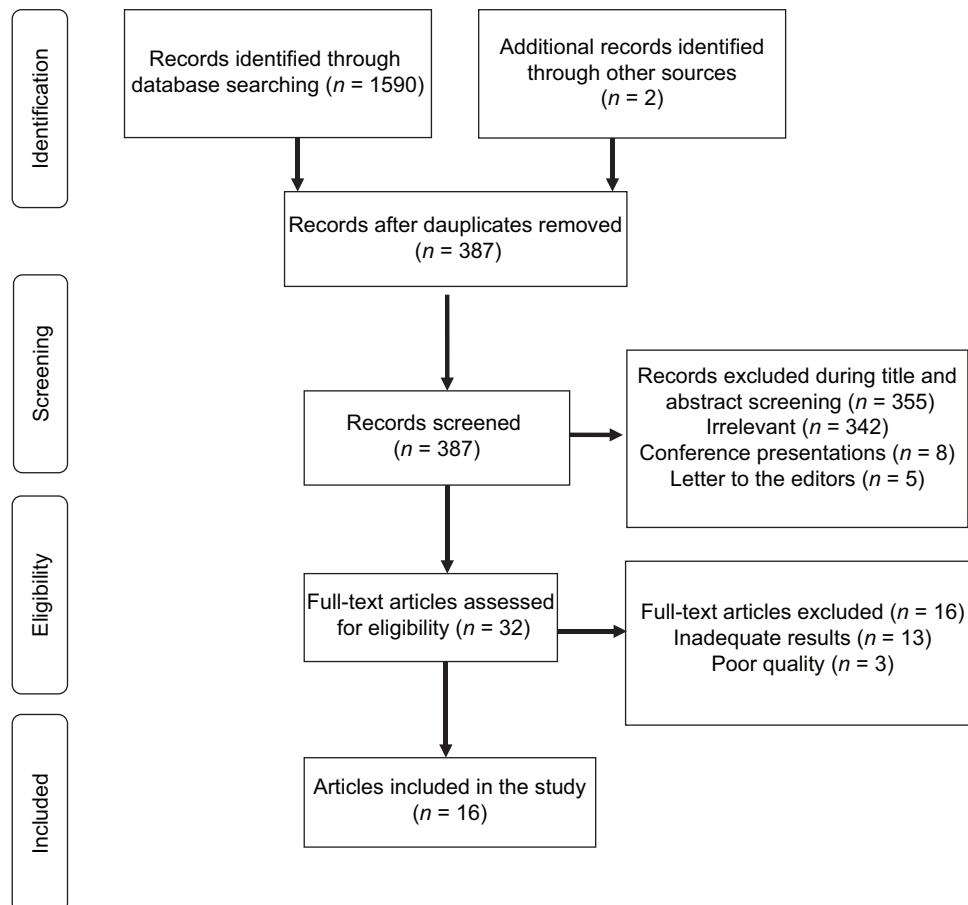


Figure 1: The flow diagram of the literature search

Table 1: The characteristics of the reviewed studies

Author (country, year)	Design, Sample size	Mean age	TCP prevalence (%)	Quality score	Author's conclusion
Bai <i>et al.</i> (Pakistan, 2018) ^[15]	Cross-sectional, 1431	26.91 ± 5.28	6.0	16	TCP in pregnancy can cause health problems for both women and their newborns. Careful monitoring of thrombocytopenic pregnant women is recommended.
Asrie <i>et al.</i> (Ethiopia, 2017) ^[16]	Cross-sectional, 217	25.67 ± 4.69	8.8	17	TCP prevalence among pregnant women is 8.8%, with greater prevalence among women in rural areas. Routine screening for TCP is needed, particularly in rural areas.
Das and Das (India, 2017) ^[17]	Prospective, 600	Ranging: 18-45 years	8.3	15	Gestational TCP is common with a prevalence of 80%. TCP screening during pregnancy is recommended.
Chauhan <i>et al.</i> (India, 2016) ^[18]	Prospective, 546	25.45 ± 3.87	8.4	16	Gestational TCP is common. Antenatal TCP screening is recommended to diagnose pathologic TCPs.
Mubarak <i>et al.</i> (Sudan, 2014) ^[19]	Cross-sectional, 179	26 ± 6.8	13.4	18	Infection with helicobacter pylori is common among pregnant women in Sudan. However, it is associated with neither anemia nor TCP
Vyas <i>et al.</i> (India, 2014) ^[20]	Cross-sectional, 4818		7.67	14	Pregnancy outcomes in TCP largely depend on TCP type. TCP caused by preeclampsia and HELLP syndrome can be associated with adverse outcomes.
Lin <i>et al.</i> (Taiwan, 2013) ^[21]	Cross-sectional, 18,384		4.3	17	Pregnant women with incidental TCP and without comorbid conditions are not at high risk for adverse outcomes.
Dwivedi <i>et al.</i> (India, 2012) ^[22]	Observational, 1150	24.48 ± 3.62	8.17	14	Careful monitoring of TCP in pregnancy is necessary for the early diagnosis and treatment of its complications.
Yazdani <i>et al.</i> (Iran, 2012) ^[23]	Cross-sectional, 4589	26.12 ± 4.97	5.2	16	Gestational TCP is the most common cause of TCP among pregnant women. However, it has no complications for women and their fetuses. Of course, it should be differentiated from TCP associated with serious conditions such as HELLP syndrome and preeclampsia.
Nisha <i>et al.</i> (India, 2012) ^[10]	Prospective observational, 1079		8.8	16	TCP does not affect the route of delivery. Progressively decreasing platelet count during pregnancy predisposes pregnant women to the risk of TCP. Thus, routine platelet count during pregnancy is recommended.
Olayemi and Akuffo (Ghana, 2012) ^[6]	Cross-sectional, 300		15.3	14	TCP prevalence was greater than what reported in developed countries probably due to undetected malaria among patients. Thrombocytopenic pregnant women need to be assessed for malaria.
Epstein <i>et al.</i> (Spain, 2012) ^[24]	Secondary analysis, 82		11.1	15	Infection with helicobacter pylori is not associated with TCP among Hispanic pregnant women.
Keihanian <i>et al.</i> (Iran, 2010) ^[4]	Cross-sectional, 150		12.66	16	Gestational TCP does not carry serious risks for pregnant women and their fetuses.
Shamoon <i>et al.</i> (Iraq, 2009) ^[25]	Prospective, 850	28.2 ± 5.9	8.0	17	Mild gestational TCP is common but happen late in pregnancy and causes no harm to mother and newborn.
Mbanya <i>et al.</i> (Cameroon, 2007) ^[26]	Cross-sectional, 1124		8.9	14	TCP is not associated with third semester or postpartum bleeding.
Modarresnejad and Motamedi (Iran, 2001) ^[27]	Cross-sectional, 1000	27.6 ± 6.1	8.8	14	TCP incidence was greater than other countries. The prevalence of TCP in pregnancy correlates with intrauterine fetal death, preeclampsia, abruptio placenta, systemic lupus erythematosus, disseminated intravascular coagulation, and the intake of methyldopa and aspirin.

TCP: Thrombocytopenia, HELLP: Hemolysis, elevated liver enzymes, and low platelets

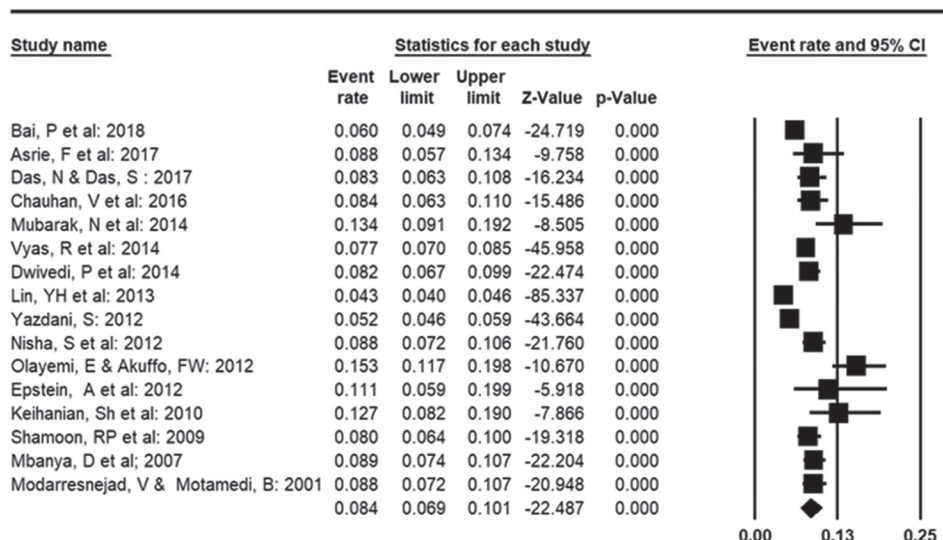


Figure 2: Prevalence of thrombocytopenia among pregnant women

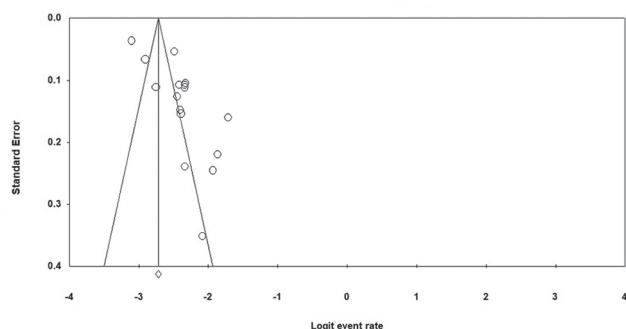


Figure 3: The funnel plot of standard error by event rate

particularly case-control studies, are needed to evaluate how different health conditions affect TCP in pregnancy.

The most common cause of TCP in the reviewed studies was gestational TCP so that a study in Iran reported it as the leading cause of 95% of TCPs among pregnant women.^[4] This rate in other studies was 85%,^[31] 81%,^[32] 92.9%,^[16] 73.8%,^[28] 70%,^[18] and 64.2%.^[10] The pathophysiology of gestational TCP is unknown; however, it is assumed that its cause may be the high consumption of platelets during pregnancy^[33] or increased plasma volume due to pregnancy.^[18] Gestational pregnancy is mild, benign, and asymptomatic, with no previous history of TCP, except in previous pregnancies. It usually happens at the end of pregnancy, is not associated with fetal TCP, and spontaneously improves after delivery.^[34] Of course, the differentiation between benign TCP and other types of TCP in pregnancy such as HELLP and preeclampsia is essential to avoid unnecessary interventions for gestational TCP and to take timely measures to manage pathologic TCPs.^[16]

Table 2: Subgroup analyses by country				
Country	Number of studies [references]	TCP prevalence (95% CI)	P	P
India	5 ^[10,19,24-26]	8 (7.4-8.6)	0.00	0.751
Other countries	11 ^[4,6,15-18,23,27-30]	8.5 (6.5-11)	94.9	<0.001

TCP: Thrombocytopenia, CI: Confidence interval

Some studies showed that TCP in pregnancy is associated with maternal and neonatal morbidity and mortality. For instance, several studies reported that 0.30%–13.20% of the neonates of thrombocytopenic women needed admission to neonatal intensive care unit.^[15,19,25] Another study on eight cases of pathologic TCP in pregnancy reported that one neonate developed cerebral hemorrhage.^[35] Therefore, careful and continuous monitoring of high risk thrombocytopenic women is needed to determine TCP etiology and take timely interventions^[18] to prevent probable complications.^[26]

Our study also revealed that there are limited studies in the area of TCP prevalence in pregnancy. Therefore, further studies are recommended to determine TCP prevalence in different areas of the world and evaluate the effects of preventive and therapeutic interventions on TCP-related outcomes among pregnant women. Moreover, routine screening and follow-up programs are needed to identify pregnant women with TCP and provide them with the necessary interventions to prevent potential fetal and maternal complications. The limitations of the present study were our limited access to some databases as well as the inclusion of only English and Persian studies. Another limitation was high possibility of publication

bias and heterogeneity in results, and readers should pay attention to this issue.

CONCLUSION

The global prevalence of TCP among pregnant women is 8.4%. In other words, around one-tenth of pregnant women in the world suffer from TCP. This high rate highlights the importance of taking diagnostic, preventive, and therapeutic measures for the management of TCP in pregnancy.

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Conflicts of interest

There are no conflicts of interest.

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