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REVIEW ARTICLE

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Vaginal bleeding in pregnancy and adverse clinical outcomes: a systematic review and meta-analysis

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ABSTRACT

Background: Vaginal bleeding during pregnancy has been recognised as a significant risk factor for adverse pregnancy outcomes. This study aimed to investigate the association between vaginal bleeding during the first trimester of pregnancy and clinical adverse effects using a systematic review and meta-analysis.

Methods: Databases of Scopus, Web of Science, PubMed (including Medline), Cochrane Library and Science Direct were searched until June of 2023. Data analysis using statistical test fixed- and random-effects models in the meta-analysis, Cochran and meta-regression. The quality of the eligible studies was assessed by using the Newcastle–Ottawa Scale checklist (NOS).

Results: A total of 46 relevant studies, with a sample size of 1,554,141 were entered into the meta-analysis. Vaginal bleeding during the first trimester of pregnancy increases the risk of preterm birth (OR: 1.8, CI 95%: 1.6–2.0), low birth weight (LBW; OR: 2.0, CI 95%: 1.5–2.6), premature rupture of membranes (PROMs; OR: 2.3, CI 95%: 1.8–3.0), abortion (OR: 4.3, CI 95%: 2.0–9.0), stillbirth (OR: 2.5, CI 95%: 1.2–5.0), placental abruption (OR: 2.2, CI 95%: 1.4–3.3) and placenta previa (OR: 1.9, CI 95%: 1.5–2.4).

Conclusions: Vaginal bleeding in the first trimester of pregnancy is associated with preterm birth, LBW, PROMs, miscarriage, stillbirth, placental abruption and placenta previa. Therefore, physicians or midwives need to be aware of the possibility of these consequences and manage them when they occur.

PLAIN LANGUAGE SUMMARY

Vaginal bleeding in the first trimester of pregnancy increases the relative risk of preterm birth, low birth weight, premature rupture of membranes, abortion, stillbirth, placental abruption and placenta previa.

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KEYWORDS
Uterine haemorrhage; vaginal bleeding; pregnancy complications; first pregnancy trimester; meta-analysis

Introduction

Vaginal bleeding during pregnancy, especially during the first trimester, can lead to adverse maternal and infant outcomes including placental abruption, premature rupture of membranes (PROMs), preterm delivery, intrauterine growth restriction (IUGR) and admission to the neonatal intensive care unit (NICU) (Madan *et al.* 2010, Sutter *et al.* 2006). Spotting and vaginal bleeding are common during pregnancy, but they have not been attributed to any specific cause (Hasan *et al.* 2010). It has that a quarter of pregnancies are associated with mild to severe vaginal bleeding during the first trimester. The prevalence of vaginal bleeding during the first trimester of pregnancy ranges from 7 to 25% (Hasan *et al.* 2010). It has been reported that about 50% of pregnant women with vaginal bleeding experienced abortion (Dongol *et al.* 2011). Generally, vaginal bleeding during the first trimester of pregnancy can predict adverse outcomes for the mother and infant and the risk of foetal, and infant mortality is quadrupled (Mustafa *et al.* 2009). These adverse outcomes can increase the rate of hospitalisation for newborns and their mothers, hinder infants' development, lead to neonatal death and impose enormous costs on the healthcare system (Dolatian *et al.* 2013, Morisaki *et al.* 2014, Nour 2012).

There is a diversity of reports regarding the association between bleeding during pregnancy and adverse neonatal outcomes, but none of them suggests a causal relationship (Dee Zhen 2017, Kayode *et al.* 2016, Yang *et al.* 2004). Differences in access to health services during pregnancy, severity and duration of bleeding, urinary tract infection,

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education level, causes of bleeding, history of abortion, unwanted pregnancy, infertility, multiple pregnancies and smoking cessation also influence the above-mentioned association and can lead to discrepancies in the results of studies. Therefore, identifying the appropriate and accurate association between bleeding during pregnancy and adverse pregnancy outcomes requires pooling studies' results and drawing a more complete picture of factors affecting pregnancy outcomes (Hasan *et al.* 2010, Nour 2012, Yang *et al.* 2004).

This systematic review and meta-analysis aimed to probe the pooled estimate of associations between vaginal bleeding during the first trimester of pregnancy and adverse clinical outcomes in the mother and infant to improve our understanding of appropriate health measures for preventing adverse pregnancy outcomes.

Methods

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) standard guideline was used to follow up the review process and report findings (Liberati *et al.* 2009).

Protocol and registration

The study protocol was registered on the International Prospective Register of Systematic Reviews (PROSPERO) under the code CRD42020167710.

Search strategy and selection criteria

This review focused on retrospective and prospective case-control and cohort studies of vaginal bleeding during pregnancy (other than spotting) and associated adverse clinical outcomes published in English-language articles (Articles with abstract or full text in English) by the June of 2023. The databases of Scopus, Web of Science, PubMed (including Medline), Cochrane Library and Science Direct were searched medical subject headings (MeSH) keywords: Uterine Haemorrhage, Pregnancy Complications, Pregnancy, stillbirth, Foetal Growth Retardation, Placenta Previa, Abruptio Placentae, Foetal Membranes Premature Rupture, abortion Premature Birth, Abortion Threatened, Premature Birth, Infant, low birth weight (LBW), Pre-Eclampsia and Apgar Score. And other relevant keywords: vaginal bleeding, adverse birth outcomes, intrauterine growth retardation, placental abruption, PROM, threatened abortion, preterm births and LBW. They were used in isolation or combination through the Boolean AND and OR operators.

Inclusion and exclusion criteria

Inclusion criteria were organised according to the Problem or Population, Interventions/exposure, Comparison and Outcome (PI(E)CO) as follows: Population: all pregnant women in the age range of 15–49 years; Intervention/exposure: vaginal bleeding during the first trimester of pregnancy (0–13 weeks); Comparison: vaginal bleeding during the first trimester of pregnancy *vs.* no vaginal bleeding; Outcome: clinical adverse outcomes including preterm birth, IUGR, LBW, preeclampsia, PROM, placental abruption, abortion, stillbirth, caesarean delivery, placental previa, Apgar score <7 at 5 min and hospitalisation in the NICU.

Exclusion criteria were studies conducted on mothers with specific types of diseases (induced pregnancy); studies on vaginal bleeding during pregnancy that did not provide required data on the estimation of the odds ratio (OR); qualitative studies, case reports, review articles and interventional studies.

Quality assessment

The researchers assessed the quality of selected studies using a scoring system based on the Newcastle–Ottawa Scale checklist (NOS) for non-randomisation studies (case-control and cohort studies). In this checklist, the 'star system' of scoring is used, and if it has high quality in the designated areas, it will be awarded a star. In cohort studies, this checklist has three parts: Selection, Comparability and Exposure, and in case-control studies, it has three parts: selection, comparability and outcome. The selection section can receive a maximum of 4 stars, the comparability section can receive a maximum of two stars and the exposure or outcome can receive a maximum of 3 stars. Total stars of 0–5, 6–7 and 8–9 were considered low quality, moderate quality and high quality, respectively. Studies with a star of upper 5 were selected for the quantitative meta-analysis process (Peterson *et al.* 2011).

Screening and data extraction

The search results were entered into Endnote version x8-1 software (Philadelphia, PA, US) and duplicate titles were removed. Then, the title and abstract of the articles were reviewed based on the inclusion and exclusion criteria, and irrelevant articles were removed. In the next step, the full text of the articles was studied by two researchers (SD and AK) and a third person as an epidemiologist. If the articles were rejected by two researchers, the reasons were mentioned, and in case of disagreement between them, the article was evaluated by the third researcher.

A checklist was used to extract data from the selected studies in terms of the sample size, study location, study years, type of study, vaginal bleeding during pregnancy, clinical outcomes associated with vaginal bleeding during the first trimester of pregnancy, the ORs and the corresponding 95% confidence interval (CI). They were used to present the clinical outcomes (pre-specified outcomes) of the present review as preterm birth *vs.* term birth, IUGR *vs.* lack of IUGR, LBW *vs.* normal birth weight, preeclampsia *vs.* lack of preeclampsia, abortion *vs.* lack of abortion, stillbirth *vs.* live birth, PROM *vs.* lack of PROM, placental previa and placental abruption *vs.* normal placenta, Apgar score less than 7 in the fifth minute *vs.* Apgar score more than 7 and admission to the NICU *vs.* non-hospitalisation. If the OR was not directly

mentioned in these studies, it was estimated by the researchers using statistical methods.

Statistical analysis

For the estimation of the OR and standard deviation (SD), the $OR = \frac{ad}{bc}$ and $SD = (OR)\frac{\ln(\text{upper limit of OR}) - \ln(\text{lower limit of OR})}{2*1/96}$ formulae were used (Tenny and Hoffman 2023). The combination of results in heterogeneous studies was performed using the random-effects model. For homogeneous studies, the fixed-effects model in the meta-analysis was used. Heterogeneity across studies was evaluated through the Q statistics and I^2 statistics with the significance level of $p < 0.10$. I^2 0–50%: not important; 50–75%: moderate heterogeneity and >75% high heterogeneity, were considered (Huedo-Medina *et al.* 2006). Sensitivity analysis was performed to investigate the influence of each study or a group of studies on the overall risk estimate at a time; for instance, studies with a small sample size or with a low-quality score were deleted. Potential publication bias was assessed through the visual inspection of Begg's funnel plot in which the log ORs were plotted against their standard errors (SEs) (Begg and Mazumdar 1994, Egger *et al.* 1997).

Results

Study selection and characteristics

The search process led to retrieving 295 articles, of which 74 and 29 were excluded, because of duplicate titles and irrelevance to the review topic. The full-text reading led to the deletion of 132 articles based on the inclusion criteria. Moreover, the lack of a clear definition of the study population, insufficient information needed to estimate the OR and the inclusion of mothers with specific types of diseases led to the deletion of 14 more articles. Finally, 46 articles were eligible criteria and included in the review (Figure 1).

A total of 46 articles with a sample size of 1,554,141 people, that were conducted between 1983 and 2023 were entered into the meta-analysis process. They included 30 cohort studies (Alijahan *et al.* 2014, Arafa *et al.* 2000, Awoleke 2012, Batzofin *et al.* 1994, Bushtyreva *et al.* 2015, Dadkhah *et al.* 2012, De Sutter *et al.* 2006, Enaruna *et al.* 2020, Hasan *et al.* 2009, Karim 1998, Khalajinia and Sadeghimoghadam 2011, Kim *et al.* 2005, Lykke *et al.* 2010, McPherson *et al.* 2013, Norman *et al.* 2010, Palatnik and Grobman 2015, Ramaeker and Simhan 2012, Riahinejad *et al.* 2011, Salim *et al.* 2020, Schuster *et al.* 2022, sengodan *et al.* 2016, Sharami *et al.* 2013, Smits *et al.* 2012, Sohrabi and Ghanbarigorgani 2010, Strobino and Pantel-Silverman 1989, Suganya and Subbarayan 2019, Williams *et al.* 1991, Yakıştıran *et al.* 2015, Yang *et al.* 2004, Yazdani *et al.* 2015) and 16 case-control studies (Addisu *et al.* 2020, Akhavan 2004, Ananth *et al.* 2006, Berkowitz *et al.* 1983, Edwards *et al.* 2012, Eskild and Vatten 2009, Guruvare *et al.* 2015, Hossain *et al.* 2007, Ishtiaq *et al.* 2014, Kayode *et al.* 2016, Lykke *et al.* 2010, Nagy *et al.* 2005, Pitaphrom and Sukcharoen 2006, Sipilä *et al.* 1992, Sun *et al.* 2012, Szymusik *et al.* 2015). Of the 46 included studies, 11 were assessed as moderate quality, 35 as high quality and none of the included studies were assessed as being of Low quality. The characteristics of the studies are described in Table S1.

Synthesis of results

The association between vaginal bleeding during the first trimester of pregnancy and PROM was investigated based on the findings of 15 studies (Addisu *et al.* 2020, Akhavan 2004, Bushtyreva *et al.* 2015, Dadkhah *et al.* 2012, De Sutter *et al.* 2006, Guruvare *et al.* 2015, Hoseini and Yaghoubipour 2012, Hossain *et al.* 2007, Ishtiaq *et al.* 2014, Lykke *et al.* 2010, McPherson *et al.* 2013, Riahinejad *et al.* 2011, Salim *et al.* 2020, Sengodan *et al.* 2016, Suganya and Subbarayan 2019) with a sample size of 92,822 women. Vaginal bleeding during the first trimester of pregnancy significantly increased PROM in pregnant women (OR 2.3, CI 95%: 1.8, 3.0). The I^2 index was reported 76.4% indicating a high degree of heterogeneity of the studies ($p < 0.001$). Therefore, the random effects model was used to analyse the data (Figure 2).

The relationship between vaginal bleeding during the first trimester of pregnancy and stillbirth was assessed using the findings of 13 studies (Akhavan 2004, Batzofin *et al.* 1994, De Sutter *et al.* 2006, Guruvare *et al.* 2015, Ishtiaq *et al.* 2014, Kayode *et al.* 2016, Lykke *et al.* 2010, Nagy *et al.* 2005, Riahinejad *et al.* 2011, Salim *et al.* 2020, Sipilä *et al.* 1992, Suganya and Subbarayan 2019, Williams *et al.* 1991) conducted between 1990 and 2020 and with a sample size of 122,297 women. It was found that bleeding during the first trimester of pregnancy significantly increased the risk of stillbirths (RR 2.5, CI 95%: 1.2, 5.0) (Figure 3).

Also, the meta-analysis of 11 studies with a sample size of 410,078 women on the assessment of the odds of preeclampsia concerning vaginal bleeding during the first trimester of pregnancy showed that the odd ratio of preeclampsia in women with vaginal bleeding during the first trimester of pregnancy was 1.5 times greater than that of women without a history of bleeding. However, this association was statistically significant (CI 95%: 1.1, 1.9). The I^2 index was reported 61.4% (Figure 4, Table 1).

Vaginal bleeding during the first trimester of pregnancy significantly increased LBW (RR 2.0, 1.5–2.6), preterm birth (RR 1.8, 1.6–2.0), abortion (RR 4.3, 2.0–9.0), placental abruption (RR 2.2, 1.4–3.3), placental previa (RR 1.9, 1.5–2.4) and admission to the NICU (RR 2.4, 1.1–4.0) (Table 1). There was no statistically significant relationship between caesarean section (RR 1.0, 0.9–1.2), IUGR (RR 1.2, 0.7–1.9), low Apgar score (RR 1.6, 0.9–2.6), and bleeding during the first trimester of pregnancy (Table 1). Regarding the relationship between bleeding during the first trimester of pregnancy and caesarean delivery, the I^2 value was 36.5% indicating the consistency between the studies. Therefore, the fixed-effects model was used for data analysis.

The symmetry of the diagram in the funnel plot indicated no publication bias (Figure 5). Also, it was not statistically significant based on the Egger test ($p = 0.24$). Meta-regression based on the gradient of the chart showed a decrease in

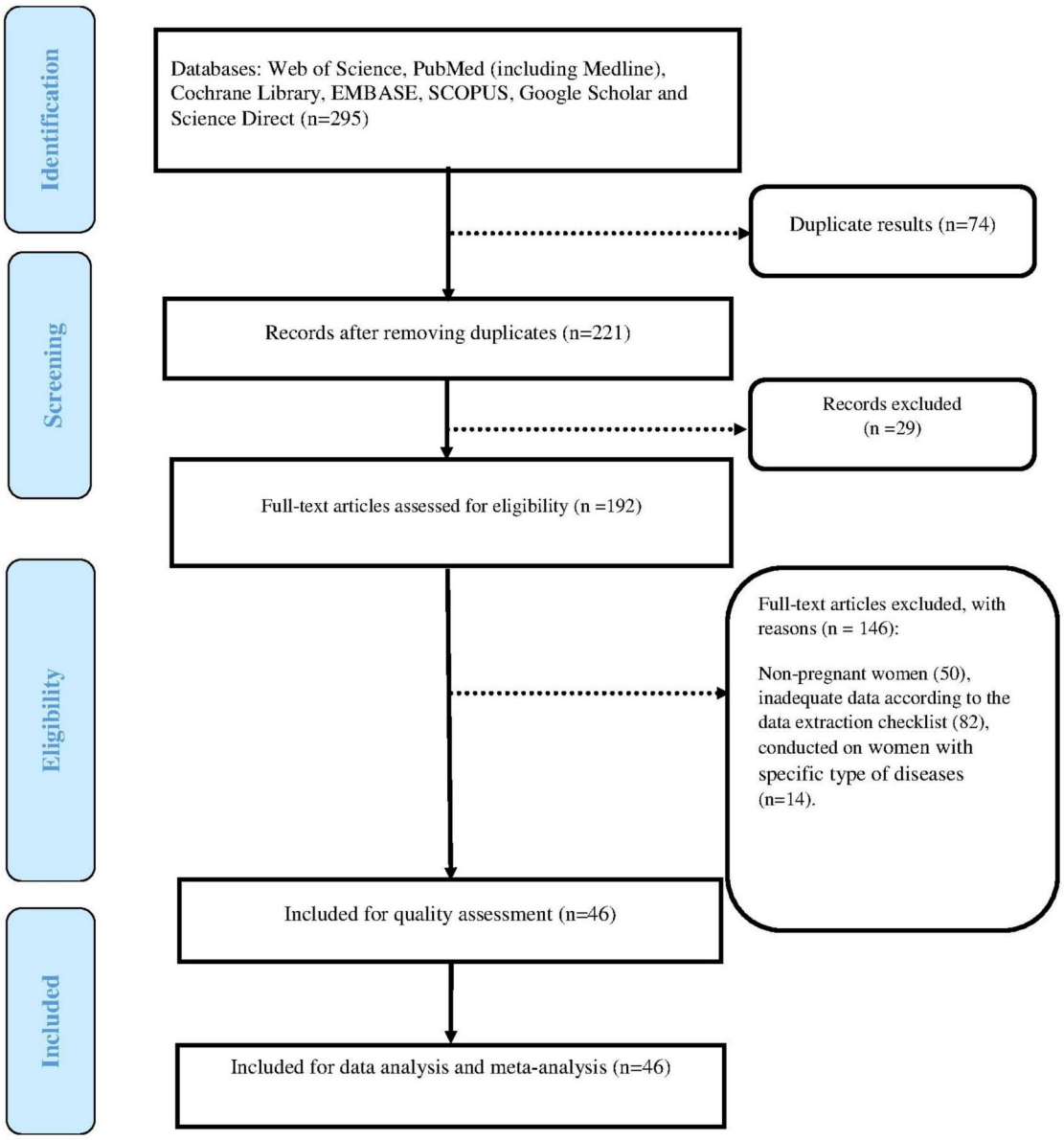

Figure 1. The PRISMA flow diagram.

relative risk with the increase in the number of studies' sample sizes, but it was not statistically significant ($p = 0.48$) (Figure 6). Sensitivity analyses to investigate whether results were changed when one study was removed at a time showed a fairly robust result after removing individual studies from the meta-analysis (data are not shown).

Discussion

This systematic review and meta-analysis were conducted with the aim of investigating the relationship between vaginal bleeding in the first trimester of pregnancy and clinical outcomes in mothers and infants. In this study, vaginal bleeding in the first trimester of pregnancy was associated with PROM. In the studies conducted, between 14% and 19.4% of women with a history of vaginal bleeding in the first trimester of pregnancy had PROM (Davari-Tanha *et al.* 2008, Hossain *et al.* 2007, Sarmalkar *et al.* 2016). In Oppenraaij *et al.*'s (2009) and Saraswat *et al.*'s (2010) review studies (OR 1.78, 95% CI 1.28, 2.48) the risk of PROM was increased in women with a history of vaginal bleeding in the first trimester of pregnancy (Oppenraaij *et al.* 2009, Saraswat *et al.* 2010). A comparison of the results of the present review with those mentioned above shows that bleeding during the first trimester of pregnancy increases the risk of PROM and can have adverse effects on the foetus. Vaginal bleeding during the first trimester of pregnancy causes placental abruption, placenta previa as well as PROM (Saraswat *et al.* 2010). PROM in pregnant women causes intra-amniotic inflammation, intra-amniotic infection, chorioamnionitis and septicaemia. It can cause distress, cord compression, necrotising enterocolitis, hypoxia and pulmonary hypoplasia in the foetus (Cobo *et al.* 2011, Dars *et al.* 2014, Shim *et al.* 2004). Therefore, the prevention of bleeding during pregnancy has a major role in the reduction of PROM and its adverse effects.

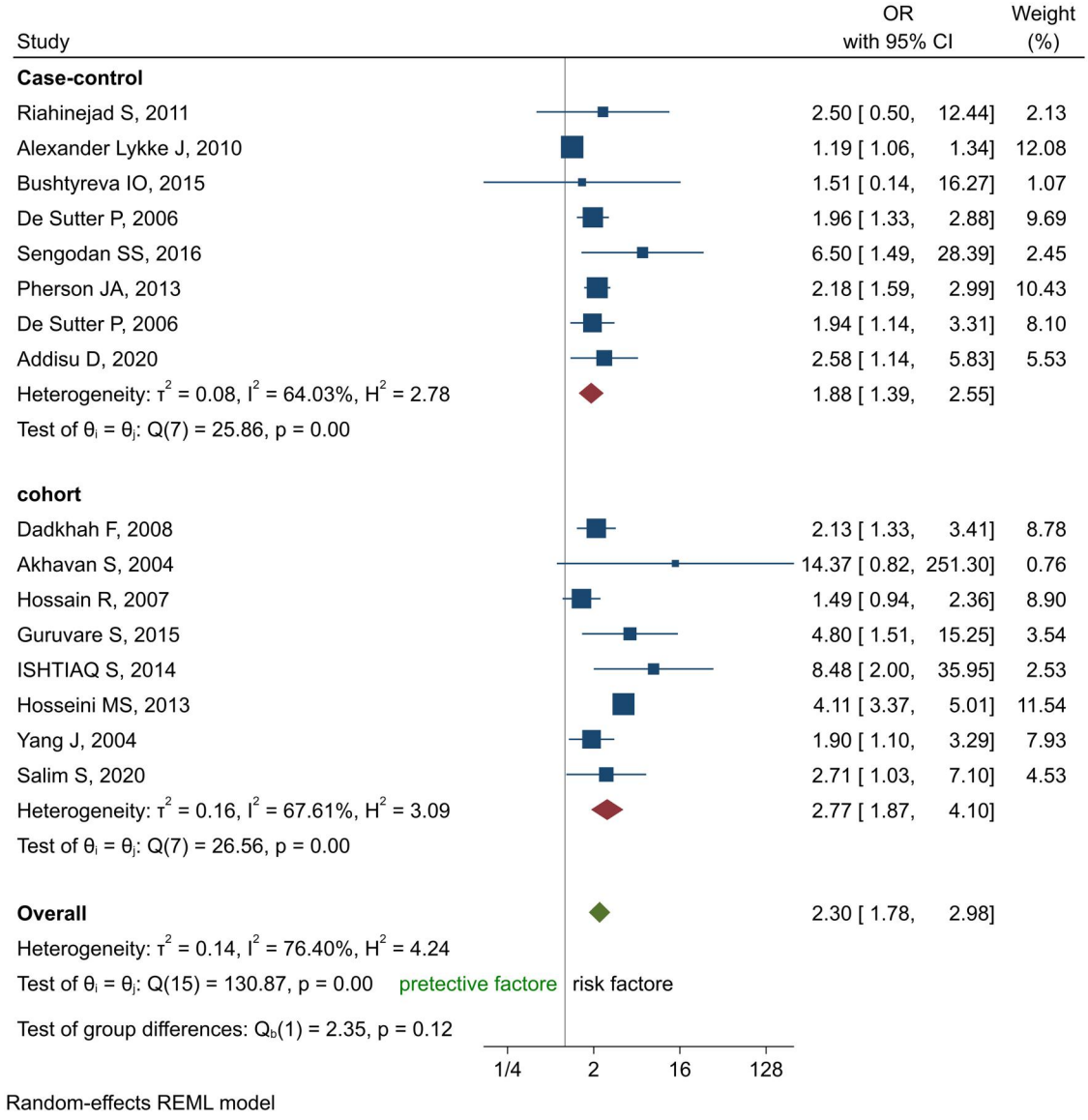

Figure 2. Forest plots of the odds ratio of vaginal bleeding during the first trimester of pregnancy with PROM and 95% confidence interval based on a random effect model in meta-analysis.

In this study, preterm delivery and LBW were more common in women with a history of vaginal bleeding in the first trimester of pregnancy. Saraswat *et al.* showed a statistically significant relationship between LBW (OR 1.83, CI 95%: 1.48–2.88), preterm birth (OR: 2.05 CI 95%: 1.76–4.2) and bleeding history during the first trimester of pregnancy (Saraswat *et al.* 2010). In other studies, the risk of preterm birth and LBW was increased in these women (Oppenraaij *et al.* 2009, Tuuli *et al.* 2011). However, multiple births, PROM and exposure to domestic violence are associated with LBW and preterm birth and can affect the relationship between bleeding and adverse pregnancy outcomes (Karimi *et al.* 2016).

Bleeding during pregnancy can be associated with PROM, placental previa, and placental abruption. At 28–34 weeks of gestation, it can lead to preterm birth and LBW (Szymusik *et al.* 2015, Tuuli *et al.* 2011, Williams *et al.* 1991, Xiao 2019, Yakıştıran *et al.* 2015). As a result, premature birth and LBW have significant effects on the infant's growth and development (Tuuli *et al.* 2011).

The results of this meta-analysis showed that placental abruption and placental previa were more common in women with a history of vaginal bleeding in the first trimester of pregnancy. However, this relationship is bilateral, and about 1% of the causes of bleeding in pregnancy are attributed to placental abruption (Baumfeld *et al.* 2017, Oyelese and Ananth 2006, Tuuli *et al.* 2011). In the conducted studies, the prevalence of placental abruption and placental previa in women with a history of vaginal bleeding is 1% and 2%, respectively, and the risk of placental abruption and placental previa in women with a history of bleeding in the first trimester of pregnancy is higher compared to other women (Amirkhani *et al.* 2013, Mulik *et al.* 2004, Norman *et al.* 2010, Oppenraaij *et al.* 2009, Sarmalkar *et al.* 2016). In a study by Tuuli *et al.* bleeding during pregnancy increases the risk of developing placental abruption by 5.7 times (Tuuli *et al.* 2011).

Our meta-analysis showed the risk of vaginal bleeding during the first trimester of pregnancy to the risk of placental

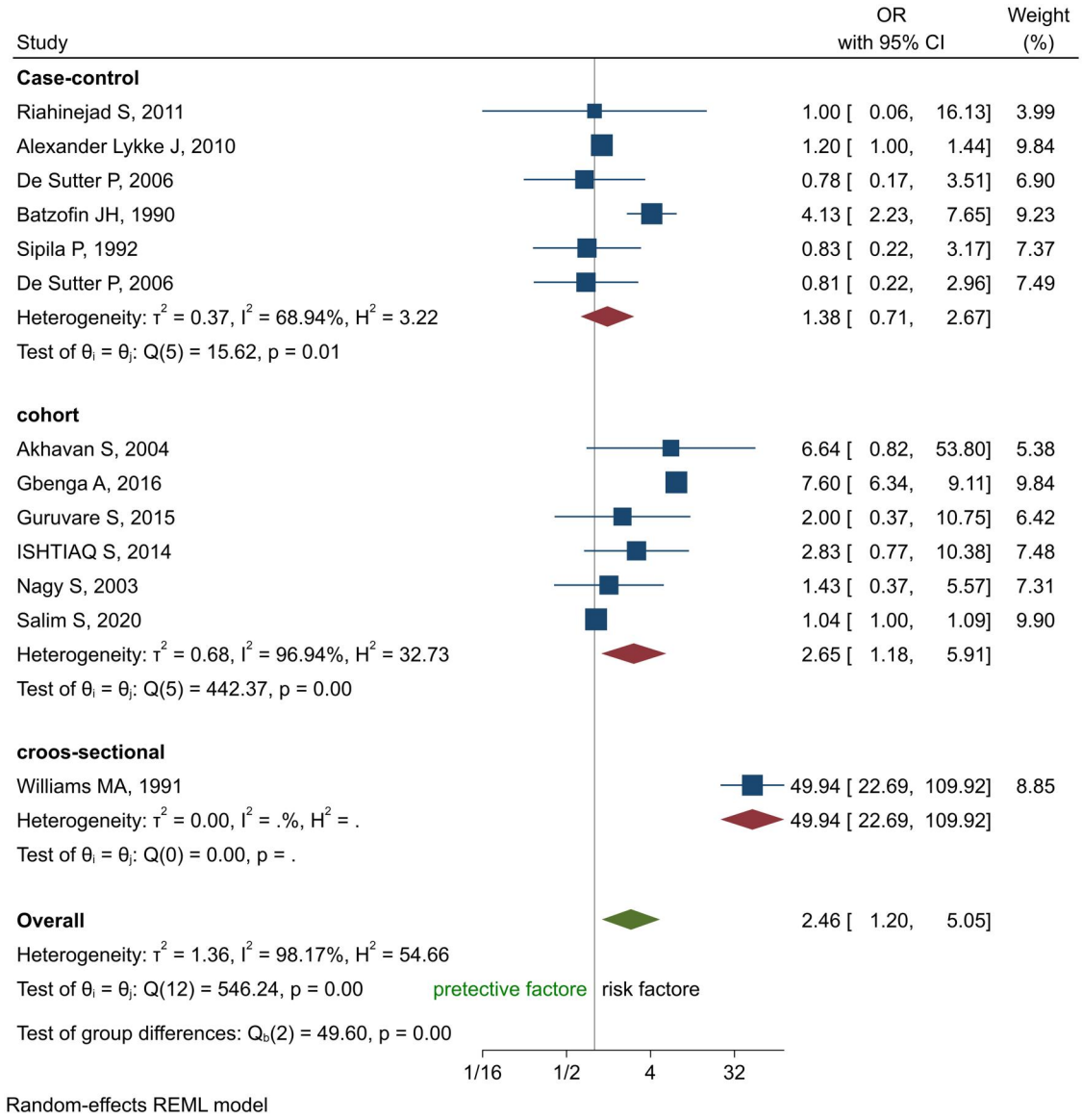

Figure 3. Forest plots of the odds ratio of vaginal bleeding during the first trimester of pregnancy with stillbirth and 95% confidence interval based on a random effect model in meta-analysis.

abruption and placental previa. In women with placental abruption, foetal death occurs in 50% of cases. Also, placental abruption and placental previa, especially in less than 34 weeks of gestation, can lead to premature birth and LBW (Ishtiaq *et al.* 2014, Williams *et al.* 1991). Accordingly, the occurrence of placental abruption and placental previa is of particular importance due to their effects on the foetus's health.

In this review, bleeding in the first trimester of pregnancy was associated with an increase in miscarriage and stillbirth. In the study of Saraswat, women with a history of bleeding during the first trimester of pregnancy had a higher rate of abortion incidents (OR: 2.15) in comparison with those women without a history of bleeding (Saraswat *et al.* 2010). This rate was 7%, 21% and 17% in the studies of Sarmalkar *et al*. (2016), Agarwal (2014) and Ahmed *et al.* (2012), respectively (Ahmed *et al.* 2012, Grawal *et al.* 2014, Sarmalkar *et al.* 2016). Tuuli *et al.* showed that bleeding during the first trimester of pregnancy increased the risk of abortion and incidence of stillbirth by 2.18 and 2.9 times, respectively (Tuuli *et al.* 2011). Bleeding during the first trimester of pregnancy causes abnormalities in the growth and development of the foetus (Bever *et al.* 2018). Therefore, as a risk factor, it can increase the probability of abortion and stillbirth, which deserves serious consideration. The fate of 50% of foetuses in women with bleeding during pregnancy due to placental abruption and placental previa is stillbirth or miscarriage. Also, PROM as a result of bleeding in the first trimester of pregnancy can lead to premature birth and miscarriage.

This meta-analysis showed no significant association between bleeding during the first trimester of pregnancy and preeclampsia, caesarean delivery, IUGR, low Apgar score and admission to the NICU. Similarly, in the study of Saraswat *et al.* (2010), preeclampsia (OR: 0.99, CI 95%: 0.84–1.17) and caesarean section (OR: 0.92, CI 95% 0.73–1.16) had no significant correlations with the history of bleeding during the first trimester of pregnancy. However, there was a significant relationship between the Apgar score of less than 7 in the fifth minute (OR

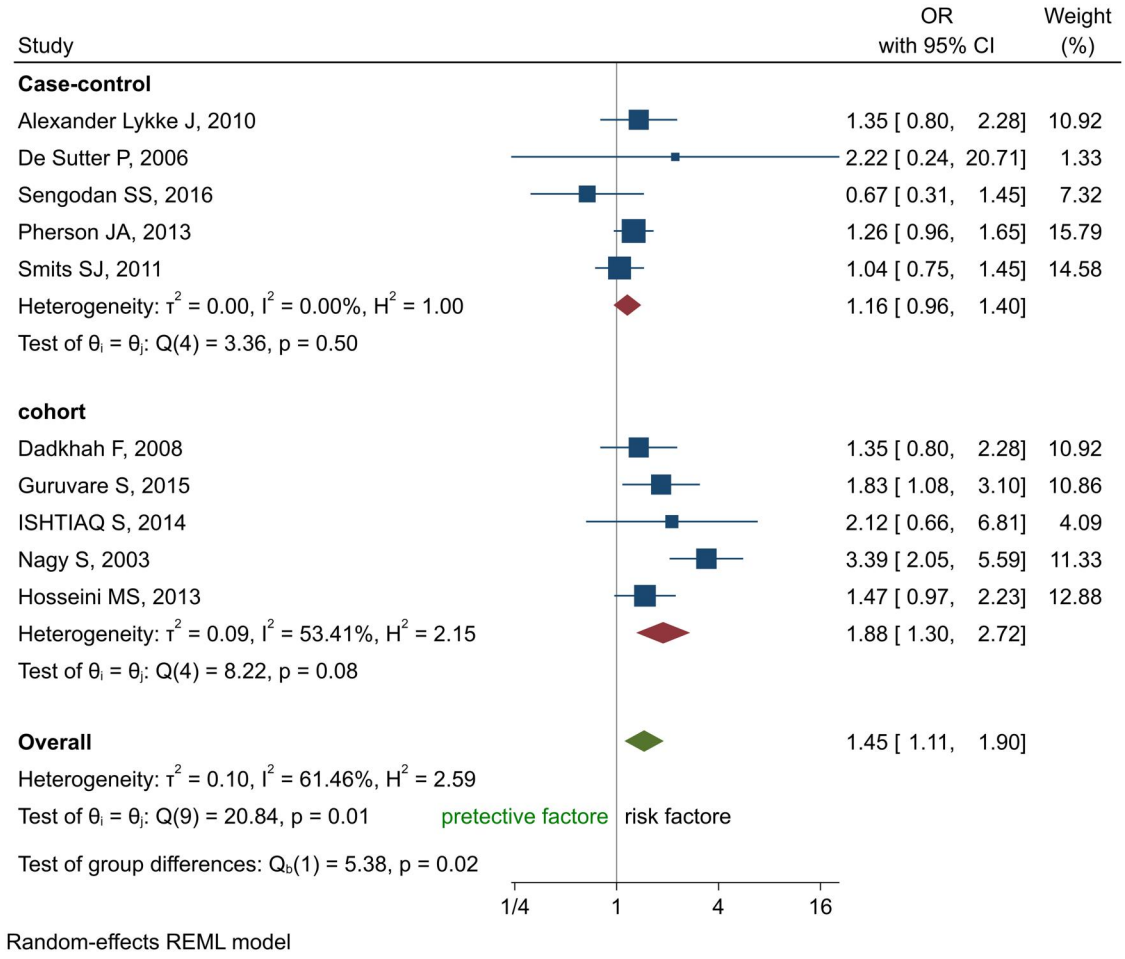

Figure 4. Forest plots of the odds ratio of vaginal bleeding during the first trimester of pregnancy with preeclampsia and 95% confidence interval based on a random effect model in meta-analysis.

Table 1. Associations between vaginal bleeding in the first trimester of pregnancy with clinical outcomes in mother and infant based on random effect meta-analysis.

	Vaginal bleeding in the first trimester of pregnancy				
Variable	*N**	*n*#	OR	CI: 95%	I Squared%
Low birth weight	16	171,855	2.0	1.5–2.6	90.58
Preterm birth	37	1,025,867	1.8	1.6–2.0	89.0
Intrauterine growth retardation	16	112,419	1.2	0.7–1.9	47.1
Preeclampsia	11	410,078	1.5	1.1–1.9	61.4
Abortion	8	72,371	4.3	2.0–9.0	93.0
Stillbirth	13	122,297	2.5	1.2–5.0	98.0
Caesarean delivery	8	12,145	1.0	0.9–1.2	36.5
Premature rupture of membranes	15	92,822	2.3	1.8–3.0	76.4
Placental abruption	11	137,987	2.2	1.4–3.3	95.0
Placental previa	9	847,966	1.9	1.5–2.4	60.0
Apgar score <7	7	18,403	1.6	0.9–2.6	86.0
Hospitalisation in the neonatal intensive care unit	6	19,566	2.4	1.1–4.0	92.8

*Number of studies; #number of samples
OR: odds ratio; CI: confidence interval

1.2, 95% CI: 1.03–1.4), IUGR (OR: 1.54 CI 95%: 1.18–2.0), admission to the NICU (OR 1.13, CI 95%: 1.03–1.23) and the history of vaginal bleeding during the first trimester of pregnancy. Inconsistency between our review results and those of Saraswat's research can be due to the lower number of included studies in Saraswat's study (Saraswat *et al.* 2010). In the study by Norman *et al.* no significant relationship was found between bleeding during pregnancy and preeclampsia as well as IUGR (Norman *et al.* 2010). In this review, although bleeding during the first trimester of pregnancy increased the risk of preeclampsia, IUGR, caesarean section, Apgar score < 7, and admission to the NICU, it was not statistically significant. Therefore, it cannot be conclusively stated that bleeding during pregnancy increases related adverse clinical outcomes.

Strengths and limitations

In our review, nearly all included studies were medium to high quality according to the NOS. Likewise, the quality of meta-analyses is mainly reliant on the quality of the original

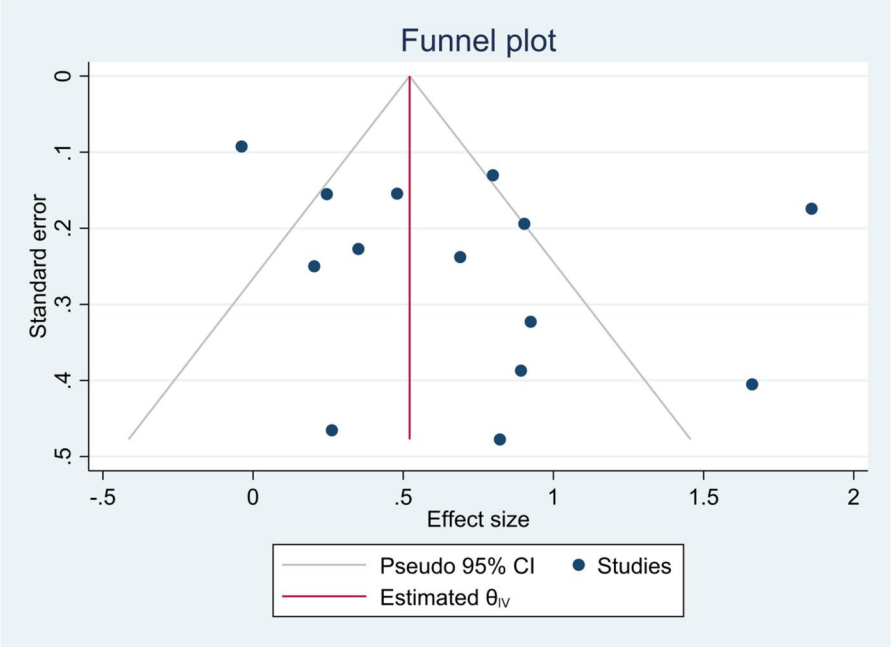

Figure 5. Funnel chart of the odds ratio in the selected studies.

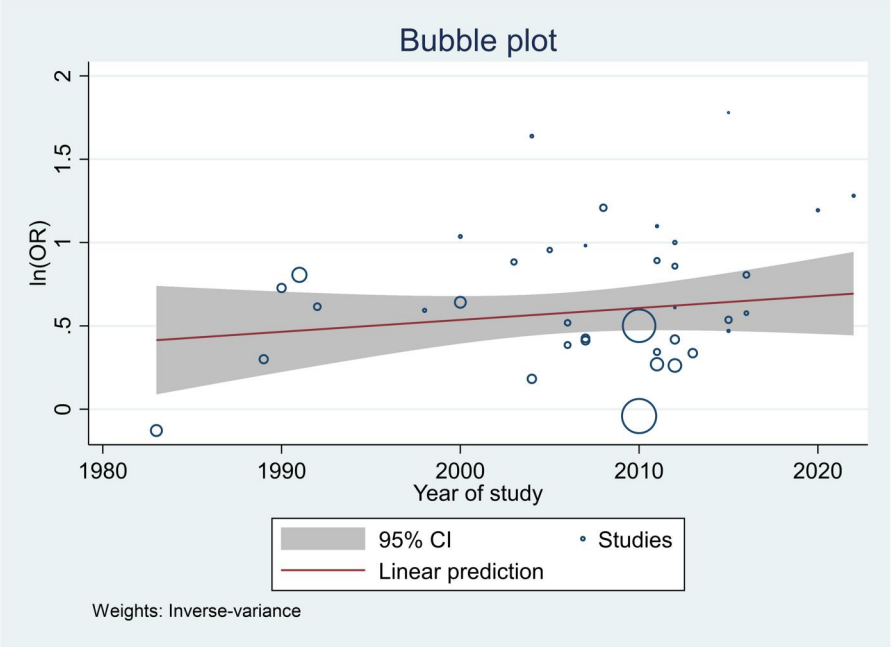

Figure 6. Meta-regression chart of the odds ratio of preterm birth upon the study year.

studies included in data analysis. The current meta-analysis included prospective cohort studies that were valuable for assessing the cause-and-effect association. Therefore, our findings can have implications for interventions aiming at the prevention of adverse pregnancy clinical outcomes. In this review, different adverse clinical effects of pregnancy were simultaneously included to avoid splitting results in different reports across the globe, which improved its generalisability. However, the following limitations should be considered during the interpretation of the findings: there was a lack of integrated definition for LBW in the studies (birth weight $<$2500 g or $<$2000 g). In this study, the weight was considered less than 2500 g. Also, in the field of premature birth, in the studies, the gestational age was reported to be less than 37 or 34 weeks, and in this study, the age was considered to be less than 37 weeks. Not reporting the OR or the information needed to estimate it, which led to the exclusion of some studies; the presence of unmatched participants, or uncontrolled confounder variables in some studies that might have affected the pooled estimates; unknown sources of heterogeneity amongst the studies.

Conclusions

Bleeding during the first trimester of pregnancy increases the chance of preterm birth, PROM, LBW, abortion, stillbirth,

placental abruption and placental previa. Hence, it is essential to identify the causes of this phenomenon and take appropriate healthcare measures to prevent bleeding during pregnancy, and pay special attention to its undesirable clinical outcomes.

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Ethics approval

This study was approved by Shahroud University of Medical Sciences (Ethical code: IR.SHMU.REC.1399.025).

Contributions to authorship

Arezoo Karimi: Data collection, data extraction, writing the manuscript, approval of the final version to be published;

Kourosh Sayehmiri: Data analysis and interpretation and quality appraisals, approval of the final version to be published;

Salman Daliri: Data collection, data extraction, writing the manuscript, approval of the final version to be published;

Mojtaba Vaismoradi: Writing the manuscript, critical interpretation of content, approval of the final version to be published;

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Data availability statement

The authors confirm that the data supporting the findings of this study are available within the article [and/or] its Supplementary materials.

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