Effect of bacterial vaginosis on preterm birth: A meta-analysis

Trishna Mohanty

Prakash Prabhakarrao Doke (prakash.doke@gmail.com)

Bharati Vidyapeeth Deemed University Medical College, Pune https://orcid.org/0000-0002-3812-002X

Sana Rafiq Khuroo

Research Article

Keywords: Pooled Odds Ratio, Pooled Relative Risk, Bacterial Vaginosis, Preterm Birth

Posted Date: July 6th, 2022

DOI: https://doi.org/10.21203/rs.3.rs-1797180/v1

Abstract

Purpose Bacterial vaginosis is a common genital tract disorder. It can lead to preterm birth but its contribution and extent is equivocal. Bacterial vaginosis is a treatable cause of preterm birth if diagnosed and treated correctly. The study desired to confirm the relationship between bacterial vaginosis and preterm.

Methods It was a meta-analysis. Articles published from 2008 to 2018 were included. The studies conducted to measure the strength of association between Bacterial Vaginosis and Preterm Birth by any statistical test were included. Studies with only conceptual aspects and qualitative data were excluded from the meta-analysis. Four search engines were identified, PubMed, Google Scholar, Cochrane, and LILAC. Forest plots were plotted separately for Odds Ratio (OR) and Relative Risk.

Results After extensive search 11 studies giving 14 relevant results with 20,894 participants were included. This meta-analysis proves that Bacterial Vaginosis is strongly associated with preterm birth. The risk of preterm delivery is >2-folds in women with bacterial vaginosis (OR, 2.79; 95% CI, 2.29 to 3.41). The combined or pooled risk ratio (RR) of pregnant women with bacterial vaginosis having a preterm birth or preterm delivery is 1.52 (RR, 95% C.I.=1.33 to 1.74).

Conclusion Our study shows a strong association between Bacterial vaginosis and preterm birth. The study concludes that investigation for bacterial vaginosis and management accordingly should be a part of the routine examination of a pregnant woman. The health system must initiate this strategy at the earliest to reduce prevalence of preterm births and thereby neonatal mortality.

Introduction

Bacterial vaginosis (BV) is the most common lower genital tract disorder among women of reproductive age [1]. The imbalance between commensal and pathogenic bacteria leads to bacterial vaginosis. In a healthy lower genital tract, *Lactobacillus crispatus* constitutes 95% of the vaginal flora; among cases of Bacterial Vaginosis (BV), *Lactobacillus crispatus* are dramatically reduced, and an overgrowth of various anaerobic bacteria exists [2–4]. In BV, there is an overgrowth of different gram-negative and/or anaerobic bacteria, such as Gardnerella vaginalis, Atopobium species., Megasphaera phylotype 1 species., Mobiluncus species., Ureaplasma urealyticum, Provetella, Peptostreptococcus, and Mycoplasma hominus [2, 5]. Bacterial vaginosis (BV) affects millions of women, is highly prevalent among low-income, urban pregnant women, and is frequently chronic [6]. The BV can be diagnosed by scoring bacterial morphotypes from a Gram stain of vaginal fluid, assigning a Nugent score between 0 and 10. A score of 0–3 represents "normal vaginal flora", 4–6 means "intermediate vaginal flora", 7–10 are considered diagnostic for bacterial vaginosis [5]. BV can be diagnosed clinically by the presence of three of the following four signs first described by Richard Amsel in 1983:

1. Presence of an adherent and homogeneous vaginal discharge.
2. A vaginal pH > 4.5.

3. Detection of clue cells (vaginal epithelial cells so covered by bacteria as to render the borders indistinct) on saline wet mount.

An amine odor (positive 'whiff test') after adding the amine potassium hydroxide (10%) to the vaginal secretions can also be predictive in the field [7]. The term vaginosis is preferred over vaginitis because of the absence of leukocytes in vaginal fluid. It can lead to other issues only during pregnancy.

Bacterial vaginosis is associated with chorioamnionitis [8], postpartum endometritis, postsurgical infections, pelvic inflammatory disease, and preterm birth. However present study focuses on preterm birth only. These Bacterial vaginosis-associated bacteria contribute to spontaneous preterm birth through localized inflammation of the endometrium creating an environment incompatible with proper placental formation and growth and/or by circulating cytokine production resulting in PPROM and subsequent Spontaneous Preterm Birth [9]. Preterm birth is defined as babies born before 37 weeks (259 days) of gestation. Based on gestational age, preterm is categorized into three groups.

1. Extremely preterm (< 28 weeks- 196 days)
2. Very preterm (28 to < 32 weeks:196–224 days)
3. Moderate to late preterm (32 to 37 weeks:224–259 days).

Despite the voluminous literature evaluating Bacterial Vaginosis and preterm birth, many doubts remain about Bacterial Vaginosis and its association with preterm birth. Its association with the most severe neonatal sequelae and the different strengths of the association between Bacterial Vaginosis and preterm birth were observed in diverse populations [1]. A few meta-analyses studies are published, but most are 15 years old.

Objective: To confirm the association between Bacterial Vaginosis and Preterm Birth through Meta-analysis.

Material And Methods

Study Setting

The study was carried out in a private medical college's Department of Community Medicine.

Study Design

It is a Meta-analysis.

Sampling Technique

We included all articles from 2008 to 2018 which satisfy selection criteria in English and another language (translated) among four search engines- PubMed, Cochrane, Google Scholar, and LILAC. We searched these search engines for the keywords "Bacterial Vaginosis" and "Preterm Birth and/or Preterm Delivery".

Inclusion Criteria

All the studies conducted for assessing association between Bacterial Vaginosis and Preterm Birth by any statistical test.

Exclusion Criteria

Studies with only conceptual data and qualitative data.

Duration of Study

1st November 2018 to 31st March 2020.

Data selection and collection

All the abstracts were read, and if found relevant, full content was viewed. In PubMed, the keywords [Bacterial vaginosis] AND [Preterm birth] were searched as MeSh. In PubMed, 110 articles were found in the last ten years, out of which 11 results had RR in their abstract and nine had OR. In Cochrane, the keyword Bacterial vaginosis and preterm birth was searched. In the last ten years, only three review articles have been published. In Google Scholar, keywords “Vaginosis, Bacterial” vaginosis AND “Preterm birth” yielded 240 results, out of which only 90 were full-text articles. Only eight results had either RR or OR. Rest 82 articles were either review articles, letters to editors, or qualitative data articles. Seven articles were repeated; they were found in PubMed as well. Articles were also received from feeds from Mendeley with the exact keywords, which yielded 20 articles. Only one article was eligible; the rest were excluded; 9 were duplicates, 6 were review articles, and 4 had qualitative data. In LILAC, 25 results were available after searching the keywords. All articles were in Spanish with English translation. None of these 25 articles were eligible as 20 didn’t mention their results, so the required data could not be extracted. Full articles could not be accessed for the rest of the five articles. Six studies had more than one result; they were counted separately and were entered independently into the excel sheet. So, finally, 22 articles were eligible for this study.

The PRISMA flow diagram in Fig. 1and 2 provides an overview of the study selection process. The investigator searched for literature, inclusion and exclusion criteria, and data extraction.

Data Analysis

The collected data were coded and entered into a Microsoft Excel sheet. Each study is summarized by estimating the effect (the result), that is, either OR or RR. Odds Ratio and Risk Ratio with a 95% confidence interval were taken from the abstract of individual studies. Following the Fixed Effect Model for meta-analysis, combined estimates from individual studies as a weighted average were calculated.

Results

The extensive search identified 14 relevant results with 20,894 participants from 11 studies [10–19].

Two studies had more than one effect size; all the respective effect sizes have been considered for those studies. We allotted a study number to each result out of 14.

Six results from four articles have RR as their effect size, and eight results from seven studies have OR as their effect size.

Two of these results were extracted for outcomes of preterm delivery at < 34 weeks. One result had the delivery outcome at 34–37 weeks, and nine had their results extracted for delivery outcomes at < 37 weeks. Two results were extracted separately from a single study for preterm birth at ≤ 34 weeks and ≤ 37 weeks. Three studies had miscarriage along with PTB as primary outcomes. Result for spontaneous preterm birth was also calculated in seven results. In one study, three different statistics were calculated for spontaneous preterm birth at < 34 weeks, 34–37 weeks, and < 37 weeks. Whereas two studies also estimated the outcome of low-birth-weight children. One study had premature rupture of membranes and abortion and PTB as primary outcomes. In one retrospective study, the primary outcomes were bacterial vaginosis, abnormal vaginal flora, and aerobic vaginitis. In another retrospective study, the association was seen between infants having five outcomes (assisted ventilation/respiratory distress at birth, admission to neonatal intensive care unit admission, neonatal sepsis, fetal mortality, and infant mortality) with exposure to Bacterial vaginosis during the antenatal period of their mother.

The inclusion criteria of different studies were bacterial vaginosis with a high-risk pregnancy, Bacterial vaginosis exposed and unexposed preterm birth and term delivery, asymptomatic pregnant women with no prior risk factor or history of Preterm delivery, pregnancy with a history of spontaneous preterm birth, preterm labor, low-risk pregnant women and women at their first antenatal visit.

Six studies used the Nugent score for the diagnosis of Bacterial vaginosis. One study has a diagnosis based on both Nugent score and real-time quantitative polymerase chain reaction assays. The diagnosis of three studies was based on lacto bacillary grades and modification of Schröder's classification. Two studies used Amsel criteria for the diagnosis of bacterial vaginosis.

Three studies did a screening at the gestational age of 20 weeks; screening was done between 6–20 weeks in one study, and another study had the screening done between 14–28 weeks. The screening was done between 10–14 weeks for two studies and between 15–27 weeks for one study. One study did a screening at 9–16 weeks and another at 20–37 weeks. Two studies did screening twice- once < 16 weeks and again between 20–24 weeks; another did the first screening at 24–37 weeks and again after more than 37 weeks.

Table 1 focuses mainly on the results of each study. Figure 3 shows the Forest plot of pooled RR of all the eligible results.

Table 1
Results of individual studies

Study no.	First author and year	Study design	Results including risk ratio (RR) or odds ratio (OR) with 95% confidence limits in brackets	
1	Krauss Silva L, 2014	Prospective Study	• (n = 1699); 42.4% of the smears collected < 14 weeks' gestation. Follow up- 8 weeks. • Nearly 40% of the initially BV positive women became BV negative. • The prevalence of BV among white women was 28.1% (24.6 to32.0%) and among black women 32.5% (28.2 to 37.2%).	The RR of spontaneous preterm delivery (PD) < 34 weeks among BV women with pH > = 4.5, as compared with those with intermediate state, were 1.24.
2	Krauss Silva L, 2014	Prospective Study		The RR of spontaneous PD 34- < 37 weeks among BV women with pH > = 4.5, as compared with those with intermediate state, were 2.49.
3	Krauss Silva L, 2014	Prospective Study		The RR of spontaneous PD < 37 weeks among BV women with pH > = 4.5, as compared with those with intermediate state, were 1.86.
4	Harper L M, 2012	Secondary analysis of a Prospective study	• Of 1453 women screened, 792 (54.5%) were diagnosed with BV. • Neither women with BV in the first trimester nor PD was at higher risk of spontaneous preterm delivery RR for BV = 1.1(0.81 to 5).	
5	Bretelle F, 2015	Prospective multicenter national study	• In 813 pregnancies, high vaginal loads of either or both of A. vaginae and G. vaginalis were associated with preterm birth [hazard ratio = 3.9 (1.1 to14.1); P = 0.031].	
6	Dingens A S, 2016	Retrospective cohort study	• BV was associated with preterm birth [RR = 1.55 (1.34 to 1.78)]. • BV was associated with an increased risk of assisted ventilation/ respiratory distress at birth [aRR = 1.28 (1.02 to1.61), NICU admission [aRR = 1.42 (1.11to 1.82)], and neonatal sepsis [aRR = 1.60 (1.13 to 2.27) among full-term infants. • Among preterm infants, BV-exposure was associated with an increased risk for NICU admissions only [aRR = 1.24 (1.04 to1.46)].	

Study no.	First author and year	Study design	Results including risk ratio (RR) or odds ratio (OR) with 95% confidence limits in brackets
7	Nelson D B, 2014	Prospective Study	• In addition, pregnant women with a prior PTD and increasing levels of Leptotrichia/Sneathia species [aOR = 9.1 (1.9 to 42.9)], BVAB1 [aOR = 16.4 (4.3 to 62.7)] or Megasphaera phylotype 1 [aOR = 6.2 (1.9 to 20.6)], through 24 weeks gestation, were significantly more likely to experience a spontaneous preterm delivery.
8	Jones N M, 2010	Pregnancy Outcomes and Community Health (POUCH) Study	• Women with a Nugent Score of ≥ 4 and the TNFα − 238 A/G or A/A were at increased risk of delivering preterm [race/ethnicity adjusted OR = 2.6; (1.2 to 5.8)].
9	Johnson H L, 2010	Case Control Analysis	• Of the pregnant women, 22% experienced an (APO) Adverse Pregnancy Outcome (7% preterm birth, 4% low birth weight, and 12% preterm birth and low birth weight). • BV is associated with PTB, OR = 1.33 (0.88 to 2.02)
10	Donders G G, 2009	Surveillance study	• Women without abnormalities of the vaginal flora in the first trimester had a 75% lower risk of delivery before 35weeks compared with women with (AVF) Adverse Vaginal Flora [OR = 0.26 (0.12 to 0.56)]. • The absence of lactobacilli (AVF) was associated with increased risks of preterm birth [OR = 2.4 (1.2 to 4.8)], early preterm birth [OR = 6.2 (2.7 to 14)] and miscarriage [OR = 4.9 (1.4 to 17)]. BV was associated with increased risks of PTB [OR = 2.4 (1.1 to 4.7)], early preterm birth [OR = 5.3 (2.1 to 12.9)] and miscarriage [OR 6.6 (2.1 to 20.9)] and coccoid AV was associated with increased risks of early preterm birth [OR = 3.2 (1.2 to 9.1)] and miscarriage [OR = 5.2 (1.5 to 17)]. • In women with BV, partial BV had a detrimental effect on the risk of preterm birth for all gestational ages, but full BV did not. • Preterm deliveries later than 24weeks + 6days were more frequent when M. hominis was present [early preterm birth, OR = 13.3 (3.2 to 55)].
11	Nejad V M, 2008	Case Control Study	• The estimated OR for positive history of preterm labour was 3.75 (1.19 to12.6; P = 0.010) by classic calculation that did not differ significantly and was 3.5 (1.3 to 9.7; P = 0.012) after logistic regression. • The obtained OR for bacterial vaginosis was 2.63 (1.03 to 6.85; P = 0.024) after decrease in logistic regression calculation.
12	Yzeiraj-Kalemaj L, 2013	Case Control Study	• A higher prevalence of bacterial vaginosis in women showing preterm labor activity, when compared with the other group, respectively, 32% and 14,6% with an OR (odds ratio) = 2.73 (1.22 to6.11; P = 0.013)

Study no.	First author and year	Study design	Results including risk ratio (RR) or odds ratio (OR) with 95% confidence limits in brackets	
13	Donders G G, 2010	Surveillance study	• Short cervix (CL below the lower quartile) at 10–14 weeks is related to a lower CL at 20–24 and 30–34 weeks of gestation (p = 0.01, p = 0.005 respectively). • Short cervix at 20–24 weeks, but not at 10–14 weeks, was predictive for preterm birth. In patients with M. hominis and/or with severe AV at 10–14 weeks, the cervix appeared shorter at 20–24 and at 30–34 weeks than in other women. • Increased risk for preterm birth in women with a shorter cervix at 10–14 weeks and AVF could not be proved by this study.	Absence of lactobacilli at the first visit at 9–15 gestational weeks was associated with an increased risk for preterm delivery ≤ 37 weeks [OR 2.3 (1.3 to 3.9); P = 0.0035].
14	Donders G G, 2010	Surveillance study		Absence of lactobacilli at the first visit at 9–15 gestational weeks was associated with an increased risk for preterm delivery ≤ 34 weeks [OR = 4.8 (2 to 12); P = 0.0027)].

The combined or pooled risk ratio of pregnant women with bacterial vaginosis having a preterm birth or preterm delivery is 1.52 (95% C.I.=1.33 to 1.74). The statistic indicates a strong association between preterm birth and bacterial vaginosis. The risk was low when RR was calculated for subgroups of studies that screened for bacterial vaginosis at < 20 weeks of gestation (1.17; 95% CI = 0.81 to 1.69). This RR is the same (1.17; 95% CI = 0.81 to 1.69) for the subgroups of studies with the primary outcome as Spontaneous Preterm Birth (SPTB).

Figure 4 shows the Forest plot of pooled Odd's Ratio (OR) of all the eligible results. The combined or pooled odd ratio is 2.79 (2.29–3.41).

The chances were higher when calculated for subgroups of studies that screened for bacterial vaginosis at > 20 weeks of gestation (odds ratio, 3.94; 95% CI, 3.03–5.13).

The author drew forest plots using Microsoft Excel rather than using SPSS software.

Discussion

There is a lack of knowledge regarding the clinical circumstances that emphasize bacterial vaginosis and preterm birth. Information is also not clear regarding the optimal time for diagnosing bacterial vaginosis and its association with obstetric and neonatal sequelae. Due to ambiguous conclusions, the only answer is a meta-analysis to assess the association between bacterial vaginosis and preterm birth. This meta-analysis includes new evidence, emphasizing different results extracted from the same study, considering retrograde studies, and identifying the interventions and outcomes.

This meta-analysis shows a strong association between bacterial vaginosis and preterm birth. Preterm is a significant health problem in India. It is among the ten countries with the most significant number of preterm birth (India, 351,900) [21]. Preterm birth or preterm delivery or prematurity is the single most important cause of death in the critical first month of life, and it is the second-leading cause of death in children under five years of age.

Preterm birth is mainly caused due to multiple pregnancies, infections, and chronic conditions such as diabetes and high blood pressure [22]. Amongst all infections, bacterial vaginosis is significant, which can cause adverse obstetric and fetal outcomes.

Few reasons have been incriminated bacterial vaginosis like, new or multiple sex partners, cervical douching, etc. can disturb the balance of vaginal microbiota [23]. Having bacterial vaginosis may elevate the risk of getting other STDs. Pregnant women with bacterial vaginosis can give rise to preterm birth or babies with low birth weight. Many cases go asymptomatic, so it's crucial to diagnose it during the antenatal period. So, screening should be done during early antenatal visits. Diagnosis is mainly made via Nugent score or Amsel criteria. If an affected pregnant woman doesn't get treated, it will increase adverse fetal outcomes, especially preterm birth. Therefore, these two variables (bacterial vaginosis and preterm birth) have been chosen to do a meta-analysis and estimate their association.

The inherent difficulties for comparison were the period of gestation of diagnosis was not uniform and the investigators have studied outcome as various gestations. Almost all the studies considered for conducting this meta-analysis favored the association between bacterial vaginosis and preterm birth. Four studies showed an intermediate risk of bacterial vaginosis causing preterm birth, and two studies showed a higher risk of getting preterm. Seven studies had a strong association between bacterial vaginosis and preterm birth, and only one study showed an intermediate association. However, two studies interpreted no association of bacterial vaginosis with preterm birth.

This meta-analysis proves that Bacterial Vaginosis is strongly associated with preterm birth. The risk of preterm delivery is > 2 folds in women with bacterial vaginosis (OR = 2.79; 95% CI, 2.29 to 3.41). Bacterial vaginosis late in pregnancy is a much stronger risk factor for preterm delivery than bacterial vaginosis infection in early pregnancy. The risk of bacterial vaginosis causing preterm delivery is four times in late pregnancy. In a meta-analysis, Harald Leitch et al. calculated higher risks for women screened for bacterial vaginosis at < 16 weeks of gestation (OR = 7.55; 95% CI, 1.80 to 31.65) or at < 20 weeks of gestation (OR = 4.20; 95% CI, 2.11–8.39). This study also had a significantly higher risk of spontaneous abortion (OR = 9.91; 95% CI, 1.99 to 49.34). The pooled OR of this meta-analysis is similar to the present study (OR = 2.19; 95% CI, 1.54 to3.12). This meta-analysis included 18 studies with 20,232 patients. They concluded that bacterial vaginosis early in pregnancy is a strong risk factor for preterm delivery and spontaneous abortion [24].

Another meta-analysis on treating abnormal vaginal flora in early pregnancy with clindamycin to prevent spontaneous preterm birth calculated the separate relative risk for spontaneous preterm birth at < 37 weeks and < 33 weeks. In both the conditions, it showed low risk. (RR at < 37weeks = 0.60; 95%; CI, 0.42 to

0.86 and RR at < 33 weeks = 0.44; 95% CI, 0.14 to1.41). they included five trials with 2346 women as study participants. They concluded that administration of clindamycin at < 22weeks of gestation was associated with a significantly reduced risk of preterm birth [25].

Flynn C A et al. did a meta-analysis to determine the magnitude of risk conferred by bacterial vaginosis during pregnancy on preterm birth. They included 19 studies. For preterm delivery, the summary OR was 1.85, 95% CI, 1.62 to 2.44. They also concluded that bacterial vaginosis was a risk factor for low birth weight (OR = 1.57; 95% CI, 1.32 to1,87), preterm premature rupture of membranes (OR = 1.83; 95% CI, 1.39 to 2.44), and preterm labor (OR = 2.19; 95% CI, 1.73 to 2.76). Pooling adjusted ORs gave a 60% increased risk of preterm delivery in the presence of bacterial vaginosis [26]. The references included in these meta-analyses were not a part of our study because they did not fit our inclusion criteria as they were old studies.

So now, we have established a definite relationship between bacterial vaginosis and preterm birth. What about the further implications? There is a lot to know about what should be done after diagnosing bacterial vaginosis, measures to prevent it, control it, and prevent reinfection during the rest of the pregnancy. There is a question of the availability of effective treatment. Various study results about antibiotic use are ambiguous.

What should be the ideal time for screening for bacterial vaginosis, the perfect gestational age of investigation? Should only pregnant women be targeted, what about non-pregnant women of their reproductive age, and what precautions should be taken. These are the issues generated through this meta-analysis.

Limitations

There are a few limitations to this meta-analysis. We did not use some acknowledged search engines as they require substantial payment. Many articles have inadequate data; hence the authors did not consider them in the meta-analysis. Every study has the limitation of non-inclusion of unpublished data to which authors don't have any access. Thus, all biases found in any meta-analysis are applicable in our study also.

Conclusion

Our study shows a strong association between Bacterial vaginosis and preterm birth. This concludes that investigation for bacterial vaginosis should be a part of routine examination of a pregnant woman.

Declarations

Acknowledgments We are thankful to Dr. Jayashree Gothankar, Professor and Head, Dr. Varsha Vaidya Professor, and Dr. Prasad Pore, Professor, Department of Community Medicine, Bharati Vidyapeeth Deemed University Medical College.

Author contributions TM initiated the study, searched references, wrote the manuscript. PPD conceptualized the study, finalized the manuscript. SRK assisted reference search and manuscript writing. All authors have approved final manuscript.

Funding There was no funding

Declarations

Conflict of interest The authors have no conflicts of interest to declare that are relevant to the content of this article.

Ethical approval After obtaining the Institutional Ethics Committee's (DCGI Regd. No. ECR/518/Inst/MH/2014/RR-17) permission, the study was conducted.

Consent to participate Not applicable.

Consent for publication Not applicable.

References

1. Guaschino S, De Seta F, Piccoli M et al (2006) Aetiology of preterm labour: Bacterial vaginosis. BJOG An Int J Obstet Gynaecol 113:46–51. https://doi.org/10.1111/j.1471-0528.2006.01122.x
2. Beigi RH, Wiesenfeld HC, Hillier SL et al (2005) Factors associated with absence of H2O2-producing Lactobacillus among women with bacterial vaginosis. J Infect Dis 191:924–929. https://doi.org/10.1086/428288
3. Fredricks DN, Fiedler TL, Marrazzo JM (2005) Molecular Identification of Bacteria Associated with Bacterial Vaginosis. N Engl J Med 353:1899–1911. https://doi.org/10.1056/nejmoa043802
4. Spandorfer SD, Neuer A, Giraldo PC et al (2001) Relationship of abnormal vaginal flora, proinflammatory cytokines and idiopathic infertility in women undergoing IVF. J Reprod Med Obstet Gynecol 46:806–810
5. Nugent,' RP, Krohn MA, Hillier3 SL (1991) Reliability of Diagnosing Bacterial Vaginosis Is Improved by a Standardized Method of Gram Stain Interpretation. J Clin Microbiol 29:297–301
6. Rauh VA, Culhane JF, Hogan VK (2000) Bacterial vaginosis: a public health problem for women. J Am Med Womens Assoc 55:220–224
7. Amsel R, Totten PA, Spiegel CA et al (1983) Nonspecific vaginitis. Am J Med 74:14–22. https://doi.org/10.1097/00006254-197811000-00023
8. Hiller S, Martius J, Krohn M et al (1988) A case-control study of chorioannionic infection and histologic chorioamnionitis in prematurity. N Engl J Med 319:972–978
9. Goldenberg RL, Hauth JC, Andrews WW (2000) Intrauterince infection and Preterm Delivery. N Engl J Med 342:1500–1507

10. Krauss-Silva L, Almada-Horta A, Alves MB et al (2014) Basic vaginal pH, bacterial vaginosis and aerobic vaginitis: prevalence in early pregnancy and risk of spontaneous preterm delivery, a prospective study in a low socioeconomic and multiethnic South American population. BMC Pregnancy Childbirth 14:1–10. https://doi.org/10.1186/1471-2393-14-107
11. Harper LM, Parry S, Stamilio DMCE et al The Interaction Effect of Bacterial Vaginosis and Periodontal Disease on the risk of Preterm Delivery. https://doi.org/10.1055/s-0031-1295644
12. Dingens AS, Fairfortune TS, Reed S, Mitchell C (2016) Bacterial vaginosis and adverse outcomes among full-term infants: a cohort study. https://doi.org/10.1186/s12884-016-1073-y
13. Bretelle F, Rozenberg P, Pascal A et al (2015) High Atopobium vaginae and Gardnerella vaginalis vaginal loads are associated with preterm birth. Clin Infect Dis 60:860–867. https://doi.org/10.1093/cid/ciu966
14. Nejad VM, Shafaie SThe Association of Bacterial Vaginosis and Preterm Labor
15. Jones NM, Holzman C, Friderici KH et al (2010) Interplay of cytokine polymorphisms and bacterial vaginosis in the etiology of preterm delivery. J Reprod Immunol 87:82–89. https://doi.org/10.1016/j.jri.2010.06.158
16. Nelson DB, Hanlon A, Nachamkin I et al (2014) Early pregnancy changes in bacterial vaginosis-associated bacteria and preterm delivery. Paediatr Perinat Epidemiol 28:88–96. https://doi.org/10.1111/ppe.12106
17. Donders GG, Van Calsteren K, Bellen G et al (2009) Predictive value for preterm birth of abnormal vaginal flora, bacterial vaginosis and aerobic vaginitis during the first trimester of pregnancy. BJOG An Int J Obstet Gynaecol 116:1315–1324. https://doi.org/10.1111/j.1471-0528.2009.02237.x
18. Johnson HL, Ghanem KG, Zenilman JM, Erbelding EJ (2011) Sexually transmitted infections and adverse pregnancy outcomes among women attending inner city public sexually transmitted diseases clinics. Sex Transm Dis 38:167–171. https://doi.org/10.1097/OLQ.0b013e3181f2e85f
19. Yzeiraj-Kalemaj L, Shpata V, Vyshka G, Manaj A (2013) Bacterial Vaginosis, Educational Level of Pregnant Women, and Preterm Birth: A Case-Control Study. https://doi.org/10.5402/2013/980537. ISRN Infect Dis 2013:
20. Donders GG, Van Calsteren C, Bellen G et al (2010) Association between abnormal vaginal flora and cervical length as risk factors for preterm birth. https://doi.org/10.1002/uog.7568. Ultrasound Obstet Gynecol n/a-n/a
21. Blencowe H, Cousens S, Oestergaard MZ et al (2012) National, regional, and worldwide estimates of preterm birth rates in the year 2010 with time trends since 1990 for selected countries: A systematic analysis and implications. Lancet 379:2162–2172. https://doi.org/10.1016/S0140-6736(12)60820-4
22. World Health Organization. Preterm birth. https://www.who.int/news-room/fact-sheets/detail/preterm-birth. Accessed 24 May 2022
23. National Center for HIV C, Hepatitis V, Prevention T, of STD Prevention D Bacterial Vaginosis-CDC Fact Sheet. www.cdc.gov/std. Accessed 24 May 2022

24. Leitich H, Bodner-Adler B, Brunbauer M et al (2003) Bacterial vaginosis as a risk factor for preterm delivery: A meta-analysis. Am J Obstet Gynecol 189:139–147. https://doi.org/10.1067/mob.2003.339
25. Lamont RF, Nhan-Chang C-L, Sobel JD et al (2011) Treatment of abnormal vaginal flora in early pregnancy with clindamycin for the prevention of spontaneous preterm birth: a systematic review and metaanalysis NIH Public Access. Am J Obs Gynecol 205:177–190. https://doi.org/10.1016/j.ajog.2011.03.047
26. Flynn CA, Helwig AL, Meurer LN (1999) Bacterial vaginosis in pregnancy and the risk of prematurity: A meta-analysis. J Fam Pract 48:885–892

Figures

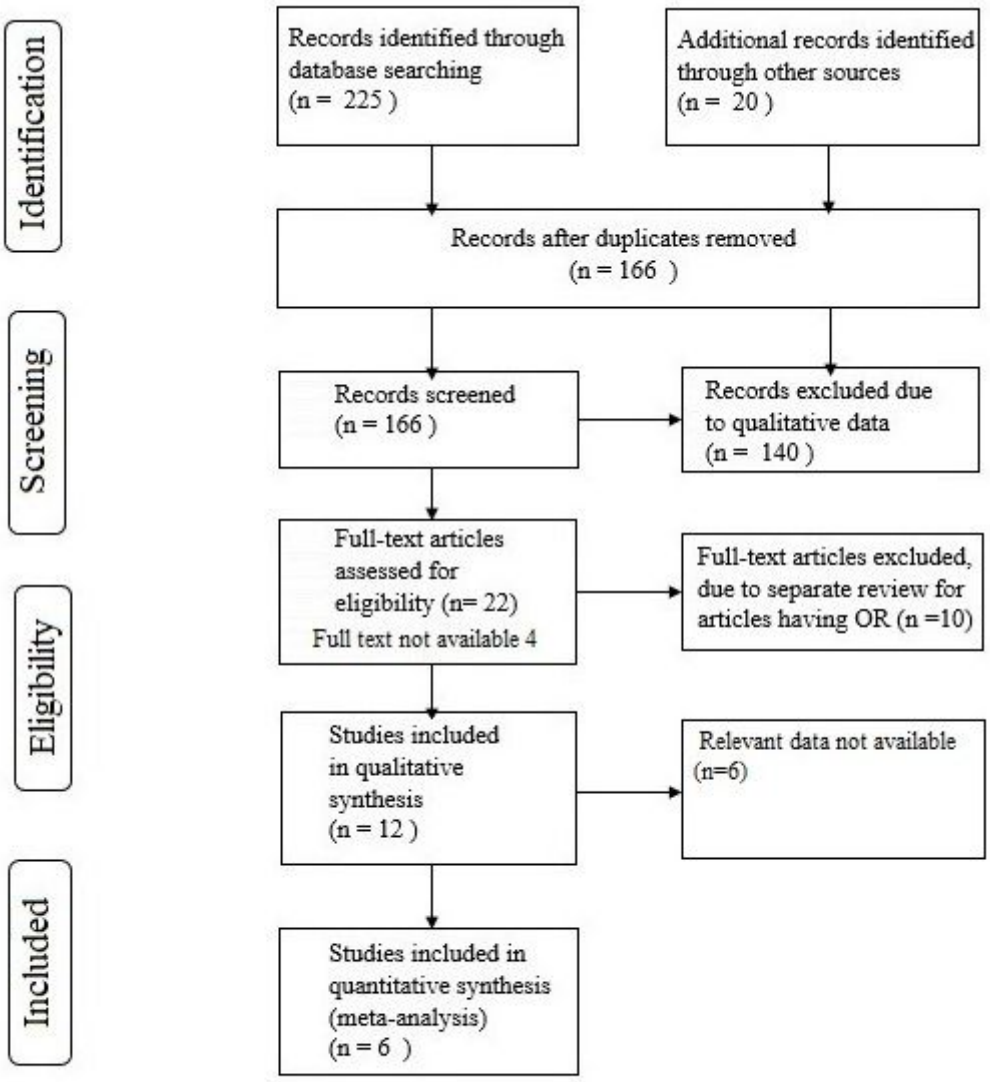

Fig.1 Flowchart of studies for risk ratio

Figure 1

Flowchart of studies for risk ratio

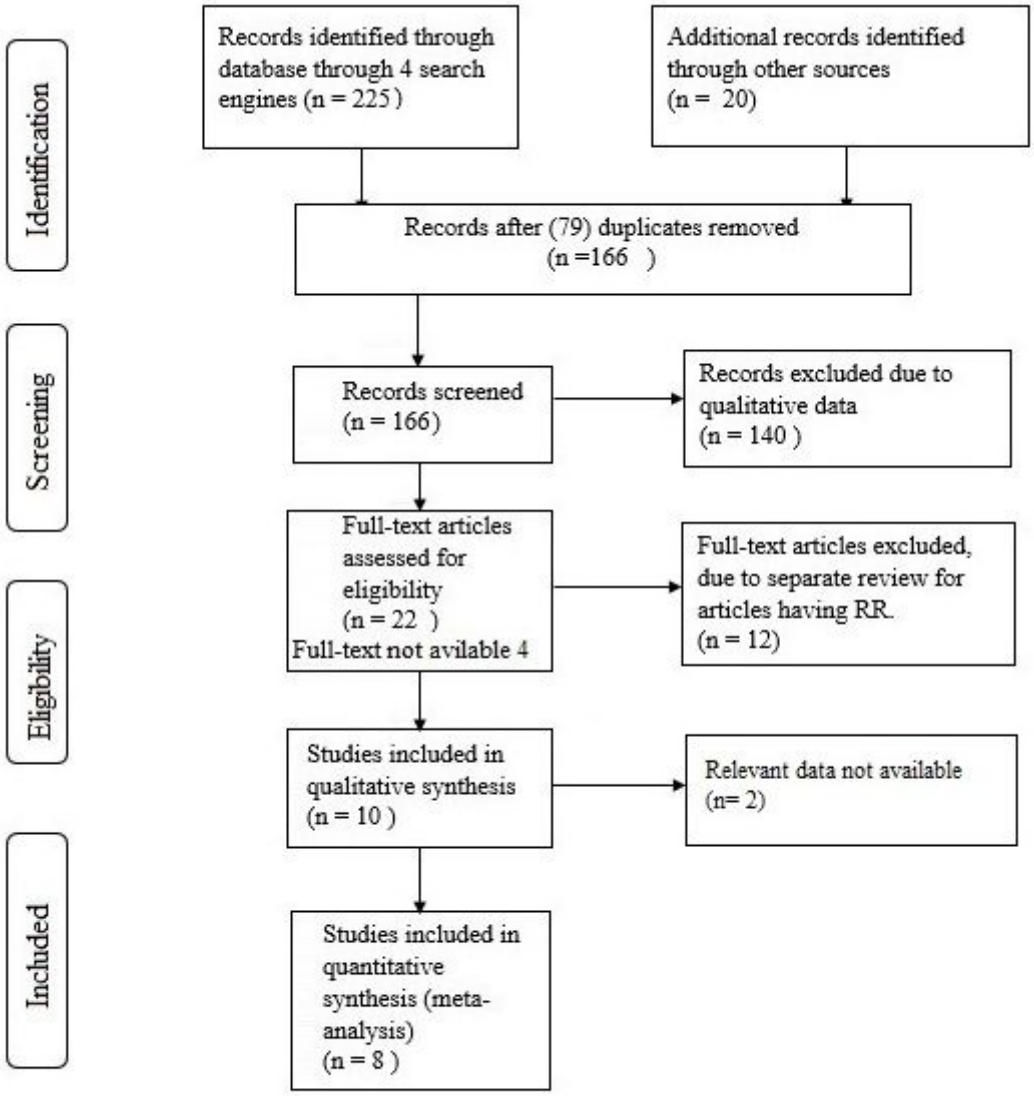

Fig. 2 Flowchart of studies for odds ratio

Figure 2

Flowchart of studies for odds ratio

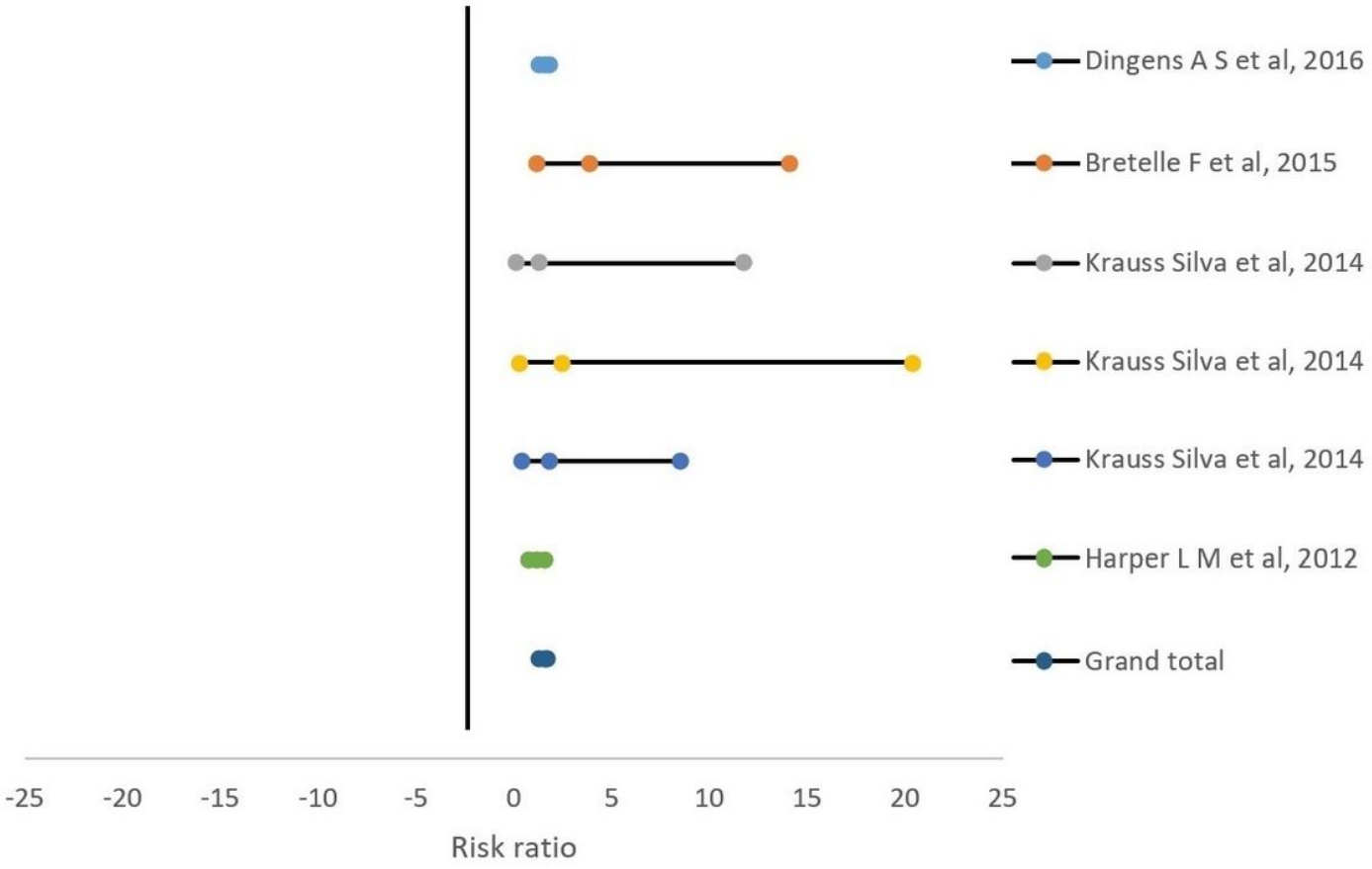

Fig. 3 Forest plot for risk ratio from various studies

Figure 3

Forest plot for risk ratio from various studies

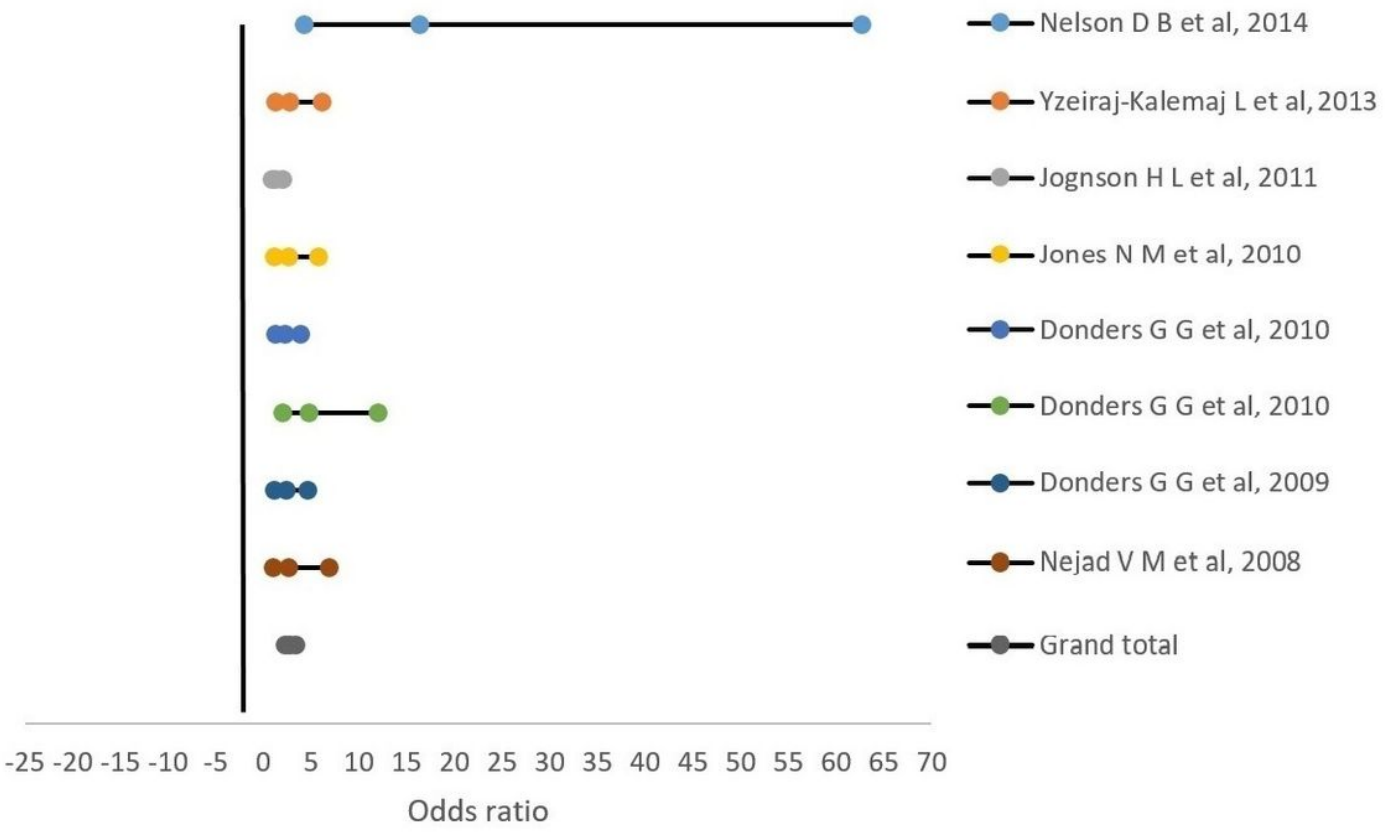

Fig. 4 Forest plot for odds ratio from various studies

Figure 4

Forest plot for odds ratio from various studies