Systematic Review

Postpartum Hemorrhage in Patients With a Low-Lying Placenta

A Systematic Review and Meta-analysis

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OBJECTIVE: We hypothesized that a second- or third-trimester diagnosis of low-lying placenta imparts underappreciated risk for postpartum hemorrhage (PPH) and placenta accreta spectrum (PAS). To quantify this risk and to assess whether it varies by the specific distance of the placenta from the cervical os and low-lying placenta resolution status, we conducted a systematic review and meta-analysis.

DATA SOURCES: Systematic searches were conducted in PubMed, ClinicalTrials.gov, EMBASE, and Web of Science from database inception to April 30, 2024.

METHODS OF STUDY SELECTION: A total of 3,700 results were screened for relevance with the PICO framework: population—singleton pregnancies; intervention—low-lying placenta; comparators—normal placentation; and outcomes—PPH and PAS. Studies published before 2000 were excluded to minimize bias from ultrasound sensitivity.

TABULATION, INTEGRATION, AND RESULTS: Twenty-one studies (3,704 patients with low-lying placenta, 2,555 with normal placentation) were included. Data extraction and quality assessment with the Newcastle–Ottawa Scale were performed independently by three reviewers. At any gestational age, low-lying placenta imparted a significant PPH risk (risk ratio [RR] 2.10, 95% CI, 1.02–4.35, P=.05, I^2=0.0%) compared with non–low-lying placenta. The incidence of PPH was 16.0% (95% CI, 10.3–24.1%, I^2=93.3%) in low-lying placenta 1–20 mm compared with 5.8% (95% CI, 3.8–8.8%, I^2=79.9%) in non–low-lying placenta. When parsed by clinically meaningfully strata, a high incidence of PPH persisted with resolved low-lying placenta (resolved: 8%, 95% CI, 4.1–16.3%, I^2=85.0%; unresolved: 29.2%, 95% CI, 19.0–42.0%, I^2=70.5%; non–-low-lying placenta: 5.8%, 95% CI, 3.8–8.8%, I^2=79.9%) with no difference in PPH risk at less than 2 cm from the os (low-lying placenta 1–10 mm: 16.6%, 95% CI, 9.2–28.3%, I^2=78.4%; low-lying placenta 11–20 mm: 17.5%, 95% CI, 8.8–31.7%, I^2=92.2%; RR 0.97, 95% CI, 0.67–1.41, P=.84, I^2=0.0%). An important finding is that PAS disorders affected 9.0% (95% CI, 4.7–16.8%, I^2=89.9%) of all low-lying placenta cases.

CONCLUSION: Antepartum diagnosis of low-lying placenta is associated with a twofold increased risk of PPH compared with normal placentation. The pooled proportions of PPH were 16.6% in the 1–10 mm group and 17.5% in the 11–20 mm low-lying placenta group, with

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no significant difference. This meta-analysis is the first to quantify the risk of PPH associated with low-lying placenta, emphasizing the need for rigorous monitoring and delivery management of pregnancies with low-lying placenta to mitigate the burden of PPH on maternal morbidity.

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Low-lying placentation is generally defined as a placenta edge located within 20 mm from the internal cervical os. Often suspected by transabdominal ultrasonography, low-lying placenta is commonly diagnosed with transvaginal ultrasonography during the second trimester and affects approximately 5% of pregnancies.[1–3] Although low-lying placenta is a common finding in early pregnancy, 0.3–0.9% of second-trimester diagnoses of low-lying placenta persist into the third trimester.[1] Recent studies have explored the risks associated with a third-trimester persistent diagnosis of low-lying placenta and the feasibility of vaginal delivery in these cases.[2,4,5] A meta-analysis by Jansen et al[2] reported successful vaginal delivery rates of 43% for an internal os distance of 0–10 mm, 85% for an internal os distance of 11–20 mm, and 82% for an internal os distance greater than 20 mm. In contrast, placenta previa, when the placenta overlies the cervical os, necessitates cesarean delivery and is a recognized risk factor for postpartum hemorrhage (PPH) and placenta accreta spectrum (PAS).[3,6,7]

Several analyses suggest that low-lying placenta may share the high morbidity risks associated with a placenta previa,[7,8] but its independent association with PPH and PAS remains largely unquantified. Meanwhile, PPH remains the leading cause of maternal morbidity and mortality worldwide.[9] Understanding the relationship between low-lying placenta and the risks of PPH and PAS is critical to guide patient counseling and management.

This systematic review and meta-analysis aims to quantify the risks of PPH and PAS accompanying an antepartum diagnosis of low-lying placenta compared with normal placentation. In addition, we aimed to determine whether the risk of PPH varies according to the distance of the placenta edge from the cervical os and whether the low-lying placenta was considered to be resolved beyond the second trimester.

SOURCES

This systematic review and meta-analysis was conducted following the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses) guidelines.[10] A comprehensive search strategy was performed across PubMed, Embase, and Web of Science from the database inception date to April 30, 2024. In addition, we conducted a search in ClinicalTrials.gov, which identified no ongoing or unpublished studies relevant to our inclusion criteria. No language restrictions were applied. Detailed search strategies and results are provided in Appendix 1, available online at http://links.lww.com/AOG/E158. We included randomized control trials, along with observational cohort and case–control studies according to the following PICO framework:

- Population–singleton pregnancies
- Intervention–second-trimester (14–27 weeks) or third-trimester (28–40 weeks) diagnosis of low-lying placenta, analyzed both according to the definition of each study and using a specific internal os distance of 1–20 mm
- Comparators–normal placentation (non–low-lying placenta)
- Outcomes–PPH and PAS

To account for changes in diagnostic capabilities of ultrasonography, studies published before 2000 were excluded during the full-text screening.

The study protocol was registered in the PROSPERO International Prospective Register for Systematic Reviews (CRD42024558043).

STUDY SELECTION

All records were imported into Rayyan, an online platform designed explicitly for study screening by multiple users.[11] Title and abstract screening and full-text screening were independently performed by two reviewers; conflicts were resolved by a third reviewer. Data extraction was independently performed by three reviewers, and conflicts were resolved by consensus reaching. The following variables were extracted from the articles:

- Study characteristics: author(s), publication year, country, institution, study design, study period, inclusion and exclusion criteria, PPH definition, and sample size.
- Low-lying placenta characteristics: study low-lying placenta definition, method of assessment, gestational age at the time of diagnosis, and follow-up for resolution.
- Population demographics: age, body mass index (BMI, calculated as weight in kilograms divided by height in meters squared), tobacco use, ethnicity, parity, and obstetric history.
- Outcomes: PPH (according to study definition), severe PPH (blood loss exceeding 1,000 mL),

estimation method to estimate blood loss, and mean blood loss. Because of limited or inconsistent reporting, data on other planned secondary outcomes (blood transfusions, retained placenta, hysterectomy, infection, length of hospital stay, and maternal death) could not be reliably extracted and therefore were not included in the quantitative synthesis.

Three independent reviewers used the Newcastle–Ottawa Scale to assess the quality of the included studies.[12] Studies were awarded one or two points for each of the eight items composing the scale, which are grouped into three domains: selection, comparability, and outcome. For studies without a control group, the selection criterion question 2 and comparability criterion question 1 were deemed not applicable. Similarly, for studies that did not report PAS rates, the selection criterion question 4 was not applicable.

Each study was graded on a scale of 0–9, with scores interpreted as follows: poor quality (0–2), fair quality (3–5), and high quality (6–9). For studies for which some Newcastle–Ottawa Scale criteria were not applicable, the total possible score was adjusted accordingly, resulting in a maximum score of 5 or 6 and in proportionally adjusted categories for those studies.

This study used R 4.4.1 for data synthesis and analysis, with the "meta" and "metafor" packages used for meta-analysis and forest plot generation.[13] All statistical tests were conducted with significance level set at 0.05. For data originally reported as medians with ranges or interquartile ranges, we used the Wan formula to convert these into means and SDs.[14] Risk ratios (RRs), pooled proportions, and pooled means were calculated with the "metabin," "metaprop," and "metamean" functions, respectively.

Given the observed heterogeneity across studies, we applied the random-effects model with the restricted maximum-likelihood estimator to account for between-study variance. The Hartung–Knapp adjustment was used to improve variance correction in random-effects CI estimation. Subgroup analyses were performed on the basis of placental distance from the cervical os and low-lying placenta resolution status. Specifically, the placental distance subgroups were categorized according to the measurements reported in each included study. Between-study heterogeneity was assessed with the χ^2 test and quantified with the heterogeneity variance (τ^2) and I^2 index. The I^2 index quantifies the percentage of total variation across studies that is attributable to heterogeneity rather than chance, with values greater than 50% indicating substantial heterogeneity.

Given the potential for between-study heterogeneity, a systematic approach was undertaken. Outlier studies were identified using influence analysis with diagnostic plots, followed by leave-one-out sensitivity analyses to assess the stability of the results. The details of the influence analysis and leave-one-out sensitivity analysis can be found in Appendix 2, available online at http://links.lww.com/AOG/E158.

To assess potential publication bias, we generated a funnel plot and performed the Egger test to detect any asymmetry suggestive of bias. A contour-enhanced funnel plot and a *P*-curve analysis were then used to differentiate true publication bias from high-level heterogeneity, both of which could lead to asymmetry in the funnel plot. The details of the publication bias analysis can be found in Appendix 2, http://links.lww.com/AOG/E158.

RESULTS

The PRISMA flow diagram (Fig. 1) represents the screening and inclusion of studies. Literature searches retrieved 3,700 citations. After duplication removal (n=1,197) and title and abstract screening (n=2,503), 87 full-text studies were reviewed, yielding 21 studies included for analysis (n=3,704 patients with low-lying placenta, n=2,555 with normal placentation).

The characteristics of the included studies are detailed in Table 1. Of the 21 studies meeting inclusion criteria, six were prospective cohort studies and 15 were retrospective cohort studies. The studies were conducted across multiple countries: the United States (five studies), Saudi Arabia (three studies), Italy (three studies), France (three studies), China (three studies), the United Kingdom (one study), Australia (one study), Canada (one study), Sweden (one study), West Bengal, India (one study), and Korea (one study) (two studies were conducted in multiple countries).

Although all studies were published after 2000, the cohorts' inclusion periods ranged from 1995 to 2021. Table 1 also provides a detailed overview of the working definitions of low-lying placenta used in each study, with gestational age at diagnosis ranging from second trimester to just before delivery. The primary outcomes assessed were PPH and PAS.

Among the 21 studies meeting a priori inclusion criteria, none were rated as poor in overall quality. Nineteen of 21 studies were judged to be of high quality, and two studies were classified as fair quality (Appendix 3, available online at http://links.lww.com/AOG/E158).

A random-effects meta-analysis of patients with a prenatal diagnosis of low-lying placenta in the second or third trimester, based on the definitions used in

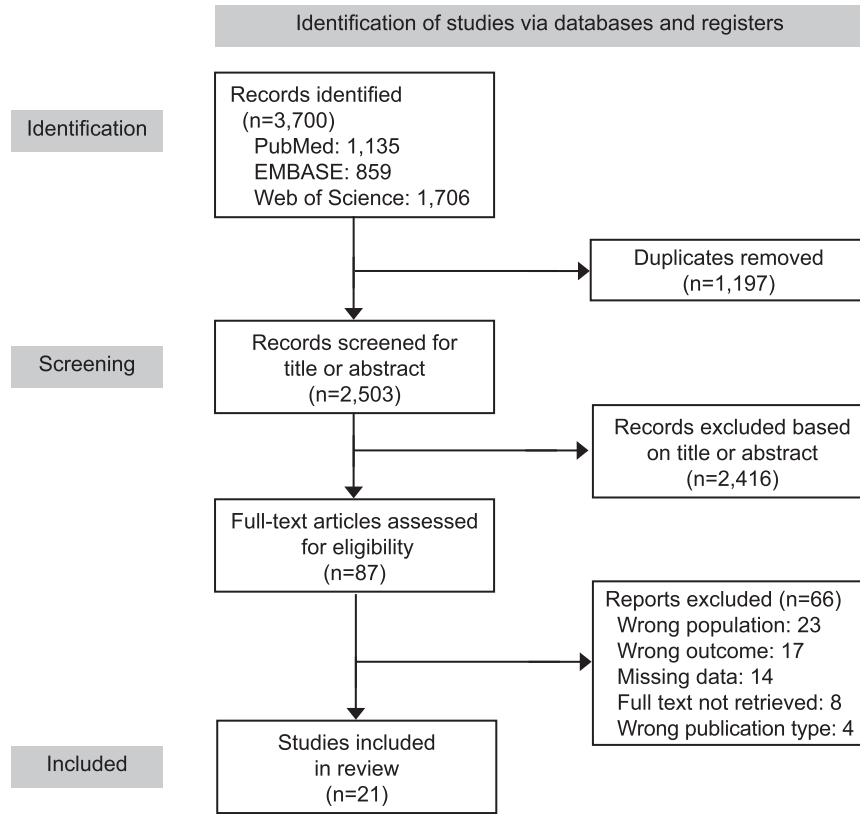

Fig. 1. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses) flow diagram of the study-selection process.

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each study (Table 1), showed a significantly higher risk of PPH compared with normal placentation (RR 1.92, 95% CI, 1.31–2.81, $P<.01$, $I^2=1.5\%$, Fig. 2A). When the analysis was restricted to studies that defined low-lying placenta using a specific internal os distance of 1–20 mm, a similarly increased risk of PPH was observed (RR 2.10, 95% CI, 1.02–4.35, $P=.05$, $I^2=0.0\%$, Fig. 2B). Sensitivity analyses did not alter the direction of these risk estimates, with the pooled estimated RR remaining above 1.0 regardless of which study was omitted. The heterogeneity analysis did not identify any outliers, and funnel plot asymmetry was not statistically significant, indicating a lack of substantial publication bias (Appendix 2, http://links.lww.com/AOG/E158). Because of insufficient data on control groups, one of the primary objectives of this meta-analysis, which was to assess the risk of PAS in patients with low-lying placenta, could not be achieved.

When we compared low-lying placenta cohorts with an internal os distance 1–10 mm and 11–20 mm, we found no significant difference in PPH risk (low-lying placenta 1–10 mm: 16.6%, 95% CI, 9.2–28.3%, $I^2=78.4\%$; low-lying placenta 11–20 mm: 17.5%, 95% CI, 8.8–31.7%, $I^2=92.2\%$; RR 0.97, 95% CI, 0.67–1.41, $P=.84$, $I^2=0.0\%$, Fig. 2C). This result remained consistent when analysis was restricted to patients with unresolved low-lying placenta, showing no significant difference in PPH risk between the 1–10 mm and 11–20 mm internal os distance groups (RR 0.97, 95% CI, 0.61–1.56, $P=.87$, $I^2=6.6\%$).

Table 2 and Figure 3 show the pooled proportions and pooled means of occurrence of PPH, mean blood loss, and frequency of PAS among different cohorts according to the internal os distance and low-lying placenta resolution status. The pooled proportion of PPH was estimated to be 5.8% (95% CI, 3.8–8.8%, $I^2=79.9\%$) among the normal placentation cohort compared with 16.0% (95% CI, 10.3–24.1%, $I^2=93.3\%$) in the low-lying placenta cohorts with an internal os distance of 1–20 mm (Table 2 and Fig. 3). Similarly, the risk of *severe PPH*, defined as blood loss exceeding 1,000 mL, was estimated to be 7.3% (95% CI, 3.3–15.4%, $I^2=87.0\%$) in the normal placentation cohort compared with 13.7% (95% CI, 7.7–23.1%, $I^2=86.1\%$) in the low-lying placenta cohorts with an internal os distance of 1–20 mm. Notably, high rates of PPH persisted even in cases in which low-lying placenta had resolved (resolved: 8%, 95% CI, 4.1–16.3%, $I^2=85.0\%$; unresolved: 29.2%, 95% CI,19.0–42.0%, $I^2=70.5\%$; non–low-lying placenta: 5.8%, 95% CI, 3.8–8.8%, $I^2=79.9\%$).

Table 1. Summary and Characteristics of the Included Studies

Study	Study Design	Country	Study Period	Inclusion and Exclusion Criteria
Ghourab, 2001[23]	Prospective cohort	Saudi Arabia	1995–2000	Inclusion: singleton, suspicion of PP or LLP Exclusion: not disclosed
Bhide et al, 2003[24]	Retrospective cohort	United Kingdom	1997–2002	Inclusion: LPP or PP diagnosed by TVUS performed for prenatal screening, antepartum hemorrhage, or abnormal presentation in 3rd trimester Exclusion: delivery in another unit (n=4)
Bahar et al, 2009[25]	Retrospective cohort	Saudi Arabia	1996–2005	Inclusion: singleton, LLP or PP after 24 GW confirmed at CD Exclusion: resolution at delivery
Vergani et al, 2009[26]	Retrospective cohort	Italy	2003–2008	Inclusion: singleton, PP with IOD 1–20 mm Exclusion: resolved PP or LLP or last US more than 28 d before delivery
Curti et al, 2012[27]	Retrospective cohort	United States, Italy	2001–2010	Inclusion: singleton, LLP in 3rd trimester, available data on cervical length Exclusion: multiple gestation
Robinson et al, 2012[20]	Prospective cohort	Australia	2007–2008	Inclusion: singleton, routine morphology ultrasonography, placenta not overlapping cervical os
Osmundson et al, 2013[18]	Retrospective cohort	United States	2009–2010	Inclusion: singleton, TVUS 18–23 6/7 wk, data groups LLP and PP Exclusion: major congenital anomalies, multiple gestations, maternal medical conditions that could predispose to PPH (eg, thrombocytopenia, anticoagulation therapy), delivery at another institution
Al Wadi et al, 2014[28]	Prospective cohort	Canada and Saudi Arabia	2010–2013	Inclusion: singleton, IOD 11–20 mm on TVUS, trial of labor Exclusion: contraindications to VD
Wortman et al, 2015[29]	Retrospective cohort	United States	2002–2012	Inclusion: 3rd-trimester LLP, marginal PP, or incomplete PP Exclusion: suspicion of placental invasion or vasa previa
Belachew et al, 2017[30]	Prospective cohort	Sweden	2010–2013	Inclusion: singleton, 1 or more previous CDs, US at 28–30 GW Exclusion: delivery before 28 wk (n=5), moved before 28 wk (n=2)
Alouini et al, 2020[31]	Retrospective cohort	France	1998–2014	Inclusion: LLP or PP in 3rd trimester Exclusion: placenta accreta or percreta diagnosed by histopathology, resolved LLP at 35 wk, lost to follow-up
Bi et al, 2021[32]	Retrospective cohort	China	2009–2019	Inclusion: TAUS or TVUS diagnosis of LLP or PP
Hong and He, 2021[33]	Retrospective cohort	China	2013–2020	Inclusion: singleton, full-term, translabial US diagnosis of LLP within 2 wk before delivery, trial of VD Exclusion: pregnancy complications, PAS, scarred uterus, uterine malformation
Ornaghi et al, 2021[5]	Retrospective analysis	Italy	2009–2018	Inclusion: singleton, LLP confirmed at 28–30 GW Exclusion: prenatally suspected PAS and vasa previa, last TVUS more than 28 d before delivery
Chandran et al, 2022[34]	Prospective cohort	West Bengal	2020–2021	Inclusion: LLP in 2nd trimester Exclusion: delivery before 32 GW, PP, PAS, resolution of LLP, lost to follow-up
DeBolt et al, 2022[17]	Retrospective cohort	United States	2015–2019	Inclusion: singleton, liveborn, PP and LLP resolved Exclusion: multiple gestations, major fetal anomaly, hematologic disorders, anticoagulation therapy, persisting LLP or PP, suspected PAS
Dong et al, 2022[35]	Retrospective cohort	China	2015–2020	Inclusion: singleton, LLP (nonresolved), vaginal delivery Exclusion: younger than age 18 y, anemia (Hb less than 110 g/L), hypertensive disorders, uterine leiomyomas, coagulation disorders

(*continued*)

Table 1. Summary and Characteristics of the Included Studies (*continued*)

Study	Study Design	Country	Study Period	Inclusion and Exclusion Criteria
Froeliger et al, 2022[36]	Retrospective cohort (multicentric)	France	2007–2012	Inclusion: LLP at "predelivery" US (nonresolved), delivery at or after 35 GW Exclusion: incomplete medical files, PP, antenatally suspected PAS, termination of pregnancy
Choi et al, 2023[37]	Retrospective cohort	Korea	2009–2021	Inclusion: nulliparous women with malpresentation, PP, or LLP who underwent CD Exclusion: multiple gestation, delivery before 20 GW, BW less than 500 g, maternal hematologic or autoimmune disease, prior myomectomy or uterine surgery, preeclampsia, eclampsia, gestational hypertension, major congenital anomalies, intrauterine fetal death, PAS, abruptio placenta
Charron et al, 2024[16]	Retrospective cohort	United States	2010–2018	Inclusion: singleton, LLP diagnosis at 18–24 GW Exclusion: major congenital anomalies, PP, vasa previa, suspected PAS, known maternal coagulopathy, intrauterine fetal death, inability to clearly image the placental edge or IOD, delivery in another unit
Kayem et al, 2024[38]	Prospective population based	France	2013–2015	Inclusion: all women with at least 1 previous CD and PP or LLP (0–20 mm from the internal cervical os, considered posterior if predominantly posterior or anterior) diagnosed by the last US before delivery Exclusion: not disclosed

Study	LLP Definition Based on IOD	PPH Definition	Sample Size	Screening Method	Gestational Age at Screening (wk)
Ghourab, 2001[23]	Less than 30 mm	Not disclosed	71 LLP	TVUS	28–32
Bhide et al, 2003[24]	Less than 35 mm	More than 500 mL after VD, more than 1,000 mL after CD	79 LLP	TVUS	21–22
Bahar et al, 2009[25]	Less than 30 mm	NA	133 LLP	Both	More than 24
Vergani et al, 2009[26]	Less than 20 mm	More than 500 mL after VD, more than 1,000 mL after CD	53 LLP	TVUS	Last US scan performed less than 28 d before delivery; mean scan-to-delivery interval 10±7.1 d
Curti et al, 2012[27]	Less than 20 mm	NA	43 LLP	TVUS	More than 28
Robinson et al, 2012[20]	30 mm or less	1,000 mL or more	464 LLP, 1,128 NP	TAUS	Median gestational age at 2nd-trimester US 19 4/7 (IQR 19 1/7, 20 0/7)
Osmundson et al, 2013[18]	25 mm or less	More than 500 mL after VD, more than 1,000 mL after CD	299 LLP, 410 NP	TVUS	Between 18 and 23 6/7
Al Wadi et al, 2014[28]	11–20 mm	Not disclosed	14 LLP	TVUS	Last formal US examination performed at approximately 37 wk; mean US-to-delivery interval 17.2±9.6 d
Wortman et al, 2015[29]	20 mm or less	More than 500 mL after VD, more than 1,000 mL after CD	98 LLP	TVUS	last formal US examination performed at approximately 34 wk
Belachew et al, 2017[30]	More than 20 mm (but close)	1,000 mL or more	24 LLP, 368 NP	TAUS	28–30
Alouini et al, 2020[31]	40 mm or less	NA	196 LLP	TVUS	31–32

(*continued*)

Table 1. Summary and Characteristics of the Included Studies (*continued*)

Study	LLP Definition Based on IOD	PPH Definition	Sample Size	Screening Method	Gestational Age at Screening (wk)
Bi et al, 2021[32]	Less than 20 mm	More than 500 mL after VD, more than 1,000 mL after CD; within 24 h from delivery	466 LLP	Both	Not disclosed
Hong and He, 2021[33]	20 mm or less	1,000 mL or less and more than 1,000 mL	80 LLP	TVUS	Within 2 wk before delivery
Ornaghi et al, 2021[5]	20 mm or less	1,000 mL or more	65 LLP, 21 NP	TVUS	28–30
Chandran et al, 2022[34]	20 mm or less	More than 500 mL	56 LLP	TVUS	2nd-trimester and 32 wk
DeBolt et al, 2022[17]	20 mm or less	1,000 mL or more or blood loss with symptoms of hypovolemia	455 LLP, 628 NP	TVUS	18–24
Dong et al, 2022[35]	20 mm or less	Not disclosed	118 LLP	TVUS	After 36 wk or within 1 wk before delivery
Froeliger et al, 2022[36]	20 mm or less	More than 1,000 mL	171 LLP	TVUS	Confirmed at predelivery
Choi et al, 2023[37]	Less than 20 mm	NA	184 LLP	Not disclosed	Not disclosed
Charron et al, 2024[16]	Less than 20 mm	More than 500 mL after VD, more than 1,000 mL after CD	503 LLP	Both	18–24
Kayem et al, 2024[38]	Less than 20 mm	Not disclosed	132 LLP	Both	Before delivery

LLP, low-lying placenta; IOD, internal os distance; PPH, postpartum hemorrhage; GW, gestational weeks; PP, placenta previa; TVUS, transvaginal ultrasound; VD, vaginal delivery; CD, cesarean delivery; NA, not available; US, ultrasound; NP, normal placentation; TAUS, transabdominal ultrasound; IQR, interquartile range; PAS, placenta accreta spectrum; Hb, hemoglobin; BW, birth weight.

To further address variability in PPH definitions across studies, we performed a subgroup analysis including only studies that consistently defined PPH as more than 500 mL after vaginal delivery or more than 1,000 mL after cesarean delivery. In this restricted analysis, the pooled proportion of PPH across all included studies (n=5) was estimated at 12.5% (95% CI, 5.3–26.8%, I^2=96.1%). Subgroup analyses based on internal os distance showed some variability: low-lying placenta 1–20 mm, 13.2% (95% CI, 4.4–33.5%, I^2=97.1%); low-lying placenta 1–10 mm, 15.4% (95% CI, 4.2–42.6%, I^2=88.7%); and low-lying placenta 11–20 mm, 14.8% (95% CI, 2.6–53.1%, I^2=97.3%) (Table 2).

The mean estimated blood loss in low-lying placenta cases was 636.12 mL (95% CI, 465.94–806.30, I^2=97.2%) and the estimated rate of PAS disorders was 9.0% (95% CI, 4.7–16.8%, I^2=89.9%).

DISCUSSION

This meta-analysis revealed that an antepartum diagnosis of low-lying placenta in the second or third trimester, including cases presumed to be resolved, is associated with a twofold increased risk of PPH compared with pregnancies that never have a diagnosis of low-lying placenta. This increased risk is consistent regardless of the proximity of the low-lying placenta to the internal os (1–10 mm vs 11–20 mm), further emphasizing the inherent risk that low-lying placenta poses and suggesting that protocols should remain consistent regardless of this classification.

When parsed by clinically meaningfully strata, significant rates of PPH persisted even in cases in which low-lying placenta had resolved by the time of delivery. Our analysis also revealed a high incidence of PAS in patients with low-lying placenta, further underscoring the substantial obstetric risks attributed to this condition.

Postpartum hemorrhage remains a leading cause of maternal morbidity and mortality worldwide,[9] making timely and accurate antenatal identification of predisposing risk factors crucial for implementing effective preventive measures. Previous research has established that placenta previa and low-lying placenta are associated with an increased risk of PPH.[15,16] Our pooled proportion of 14.9% (95% CI, 9.9–21.7%) for PPH in patients with low-lying

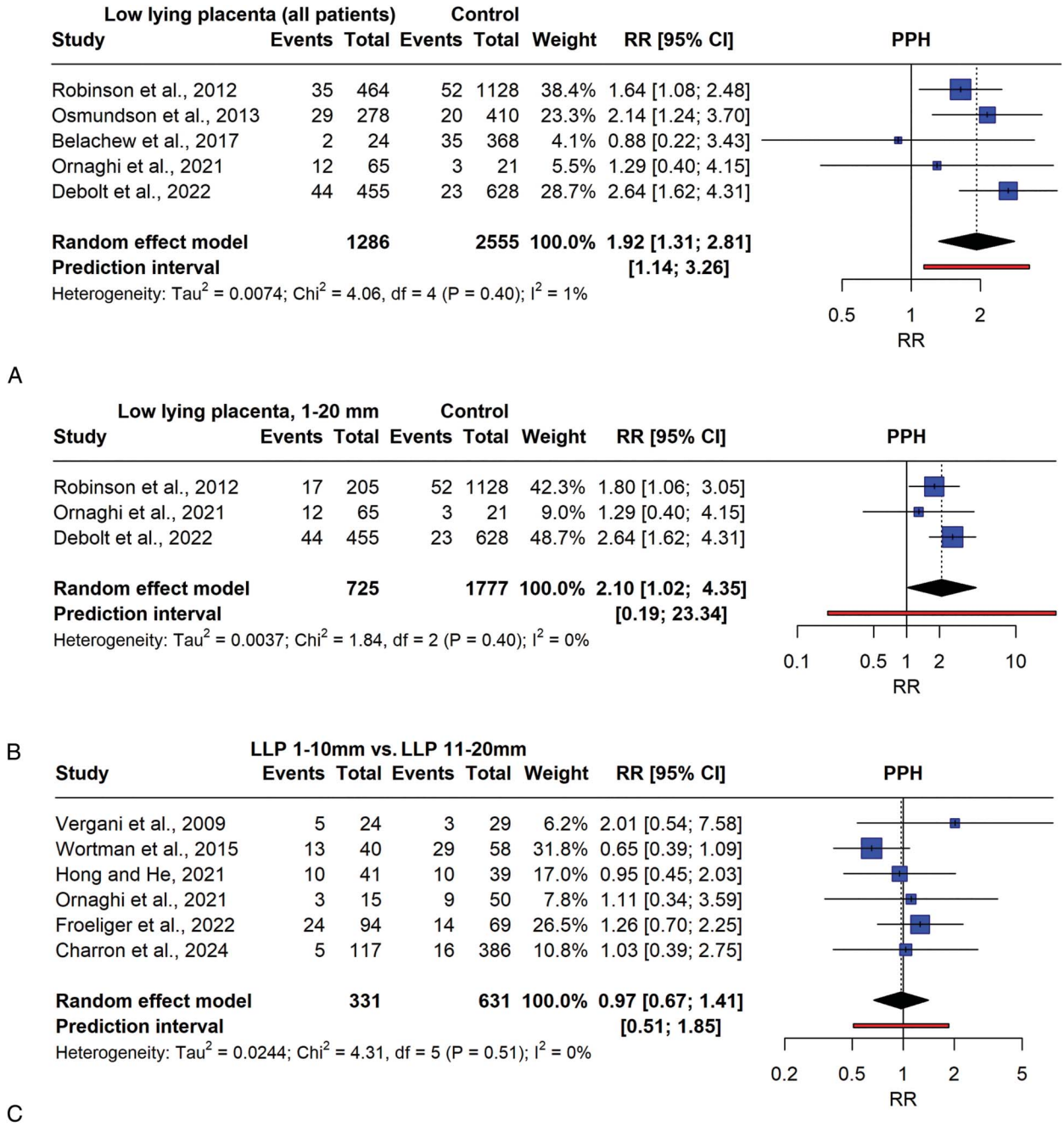

Fig. 2. Forest plots of relative risk (RR) for postpartum hemorrhage (PPH) in all patients with low-lying placenta (LLP), regardless of study definition, based on internal os distance (IOD) compared with normal placentation (**A**), defined as 1–20 mm IOD compared with normal placentation (**B**), and 1–10 mm vs 11–20 mm IOD (**C**). df, degrees of freedom.

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placenta closely aligns with the findings of a 2017 meta-analysis by Fan et al,[15] which reported an estimated rate of 15% (95% CI, 7–22%). Our study is the first meta-analysis to quantify the RR of PPH in these patients compared with patients with normal placentation, underscoring the importance of rigorous monitoring and delivery management in pregnancies with low-lying placenta to mitigate the risk of PPH and its influence on maternal health.

The literature provides conflicting evidence on the risk of PPH in women with resolved low-lying placenta before delivery. Although some studies

Table 2. Pooled Proportions and Pooled Means for Occurrence of Outcomes in the Analyzed Cohorts*

Outcome	PPH (Study Definition), PP			PPH (More Than 500 mL if VD or More Than 1,000 if CD), PP			PPH (More Than 1,000 mL), PP		
	No. of Studies	PP or PM (95% CI) (%)	I^2 (%)	No. of Studies	PP or PM (95% CI) (%)	I^2 (%)	No. of Studies	PP (95% CI) (%)	I^2 (%)
LLP cohort	15	0.149 (0.099–0.217)	93.0	5	0.125 (0.053–0.268)	96.1	5	0.131 (0.078–0.212)	82.0
Normal placentation cohort	5	0.058 (0.038–0.088)	79.9	—	—	—	3	0.073 (0.033–0.154)	87.0
LLP 1–20 mm	13	0.160 (0.103–0.241)	93.3	4	0.132 (0.044–0.335)	97.1	4	0.137 (0.077–0.231)	86.1
LLP 1–10 mm	7	0.166 (0.092–0.283)	78.4	3	0.154 (0.042–0.426)	88.7	3	0.203 (0.115–0.333)	33.5
LLP 11–20 mm	7	0.175 (0.088–0.317)	92.2	3	0.148 (0.026–0.531)	97.3	3	0.179 (0.125–0.251)	0.0
Resolved LLP	3	0.084 (0.041–0.163)	85.0	2	0.080 (0.022–0.248)	89.3	2	0.093 (0.071–0.122)	0.0
Unresolved LLP	4	0.292 (0.190–0.420)	70.5	—	—	—	—	—	—

Outcome	Blood Loss (mL), PM			PAS Disorders, PP		
	No. of Studies	PM (95% CI) (%)	I^2 (%)	No. of Studies	PP (95% CI) (%)	I^2 (%)
LLP cohort	7	636.12 (465.94–806.30)	97.2	6	0.090 (0.047–0.168)	88.9
Normal placentation cohort	—	—	—	—	—	—
LLP 1–20 mm	6	553.07 (457.95–648.19)	89.6	4	0.122 (0.065–0.217)	90.6
LLP 1–10 mm	3	582.30 (306.67–857.94)	88.2	—	—	—
LLP 11–20 mm	3	540.22 (400.26–680.19)	61.7	—	—	—
Resolved LLP	—	—	—	—	—	—
Unresolved LLP	2	553.99 (383.10–724.88)	95.1	2	0.100 (0.039–0.232)	81.8

PPH, postpartum hemorrhage; PP, pooled proportion, VD, vaginal delivery; CD, cesarean delivery; PM, pooled mean; PAS, placenta accreta spectrum; LLP, low-lying placenta.

* The analysis includes PPH as defined by study criteria (Table 1), PPH defined as blood loss more than 500 mL if VD or more than 1,000 mL if CD, and PPH defined as blood loss more than 1,000 mL. Cohorts include all patients with LLP, resolved and unresolved LLP, and subcategories based on internal os distance.

report an increased risk of PPH in this group,[8,16–21] Magann et al[22] reported a lower rate of PPH in women with resolved low-lying placenta compared with women with normal placentation. Our findings align with and confirm the majority of published studies, indicating that women with resolved low-lying placenta continue to experience substantial rates of PPH.

This meta-analysis benefits from a comprehensive search strategy, rigorous selection criteria, and stratified analysis based on placental proximity and resolution status. Notably, no low-quality studies, significant outliers, or evidence of publication bias was identified. Although a funnel plot was included to assess potential publication bias, its reliability is inherently limited by the small number of studies analyzed (less than 10). To reduce bias associated with earlier, less-sensitive ultrasound techniques, we included studies published from 2000 onward. However, three studies (Ghourab et al,[23] Bhide et al,[24] Bahar et al[25]) included patients diagnosed before 2000. Because these studies lacked a normal placentation group, they were excluded from the primary meta-analysis and were incorporated only into the calculation of pooled proportions, ensuring that they did not influence the primary outcomes. To assess their influence on pooled estimates, a sensitivity analysis was conducted, and a summary of the pooled estimates before and after exclusion is provided in Appendix 2, http://links.lww.com/AOG/E158.

The absence of a dose–response effect, whereby closer proximity to the cervix (1–10 mm) would be expected to confer a higher risk of PPH, might indicate that the pathophysiologic mechanisms underlying PPH in low-lying placenta are more complex than a direct mechanical effect. It is possible that the

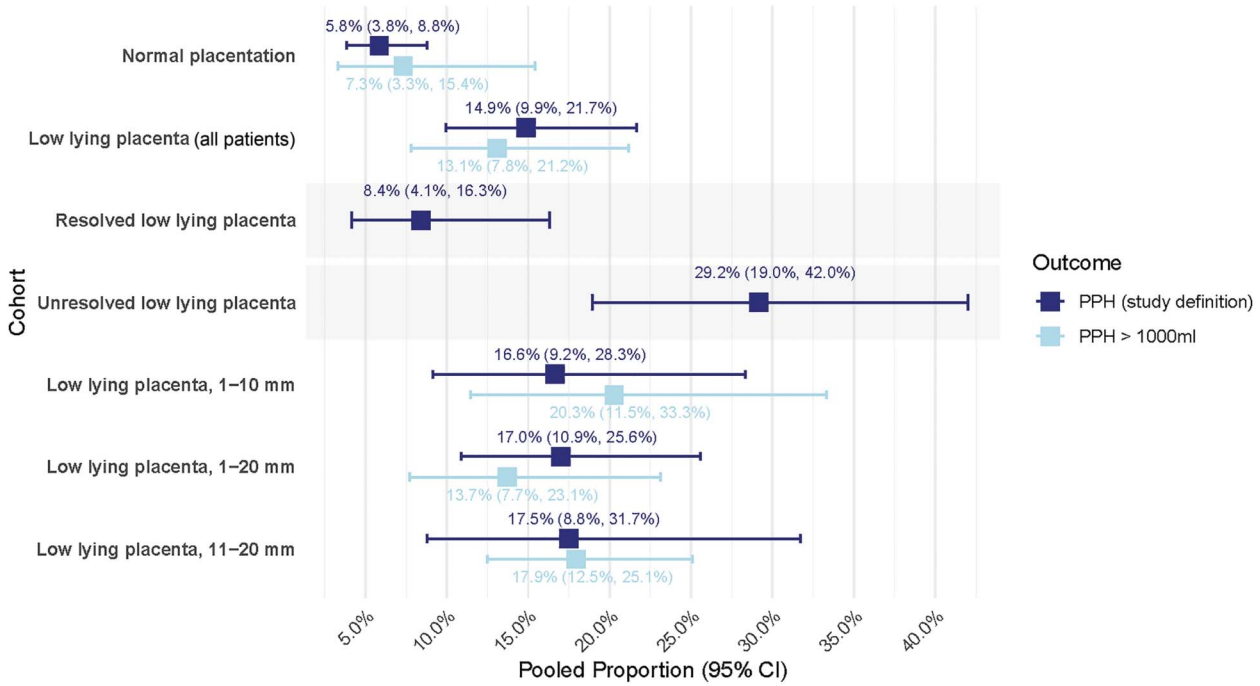

Fig. 3. Pooled proportions of postpartum hemorrhage (PPH) across different cohorts. The analysis includes PPH as defined by study criteria (*dark blue*; Table 1) and defined as blood loss exceeding 1,000 mL (*light blue*). Cohorts include all patients with low-lying placenta, resolved and unresolved low-lying placenta, and subcategories based on internal os distance.
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biological mechanisms underlying PPH in low-lying placenta are not solely dependent on the absolute distance from the cervix but rather reflect other placental or uterine factors (eg, abnormal placentation, increased vascularity, local myometrial changes). In addition, the limited number of studies directly comparing these subgroups may have influenced our ability to detect such a gradient. Future studies incorporating advanced imaging techniques such as Doppler ultrasonography or magnetic resonance imaging may provide more insights into whether low-lying placenta serves as a proxy for a higher-risk uterine environment rather than an independent risk factor for PPH.

Although one of the primary objectives of this meta-analysis was to assess the risk of PAS in patients with low-lying placenta, this could not be achieved because of insufficient data on control groups. This limitation highlights the need for future studies to include more comprehensive data on PAS risk in low-lying placenta cohorts, especially when comparing placental location and proximity to the internal os.

Variability in the definition of PPH and differences in clinical management across studies pose limitations. There was notable heterogeneity in the gestational age at low-lying placenta diagnosis, which ranged from as early as 18 weeks of gestation to as late as 1 week before delivery. To address this, we provided detailed gestational age data for each study in Table 1 and conducted a thorough sensitivity analysis to assess any significant heterogeneity or outliers in the results. The leave-one-out sensitivity analysis for low-lying placenta 1–20 mm results revealed that each individual study has a considerable influence on the pooled estimate, as evidenced by significant increases in τ^2 and wider CIs when each study was omitted. However, these omissions did not dramatically alter the direction or overall risk estimate, with the pooled estimated RR remaining above 1.0 regardless of which study was omitted. The high heterogeneity observed in some subgroups confirms the need for standardized definitions of low-lying placenta and PPH and standardized protocols for diagnosis and clinical management. In addition, the mode of delivery, which was often not reported, is an important factor that could influence PPH risk, and this underscores the importance of future research that systematically includes and reports mode of delivery along with other key factors such as gestational age at diagnosis and management protocols.

This meta-analysis provides robust evidence of the increased maternal risks in pregnancies complicated by low-lying placenta. The results highlight the need for data that define gestational ages at which low-lying placenta can be considered physiologic and when it poses increased risk for adverse outcomes, as well as mitigation strategies in antenatal and intrapartum management. Although low-lying placenta alone may not dictate delivery planning, awareness of its potential association with PPH underscores the importance of proactive third-stage management strategies, including active management of labor, early administration of uterotonics, and readiness for transfusion if necessary. Future research focused on enhanced surveillance, individualized clinical management, and shared decision making–especially for cases unresolved in the third trimester–may improve maternal safety and outcomes by facilitating timely interventions and appropriate delivery planning.

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