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PREGNANCY

BRIEF REPORT

Delivery outcomes associated with resolved first-trimester low placentation

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Abstract

Introduction: The majority of low placentation identified on first-trimester transabdominal ultrasound resolves; however, whether this resolution is associated with adverse outcome remains poorly understood. This investigation aimed to determine whether patients with resolved first-trimester low placentation had different delivery outcomes compared to patients who never had low placentation.

Methods: This is a retrospective cohort study of singleton pregnancies with low placentation, defined as low-lying placenta or placenta covering the internal os, on first-trimester transabdominal ultrasound between 12+0 weeks and 13+6 weeks, delivering at a single tertiary care center from January to December 2022. We compared outcomes stratified by first-trimester low placentation that resolved by the second trimester, or those without low placentation at any point. The primary outcome was quantitative blood loss at delivery by volumetric measurement. Secondary outcomes included postpartum hemorrhage (PPH) defined as blood loss ≥1000 cc, unplanned cesarean delivery, preterm birth, 5-min Apgar < 7, and composite maternal adverse outcomes including the use of atony device, retained products of conception, blood transfusion, peripartum hysterectomy, intensive care unit admission, or death.

Results: This cohort included 437 low placentation patients and 491 patients without low placentation. Resolved first-trimester low placentation was associated with a significant increase in quantitative blood loss at delivery (405 ± 369 cc vs. 331 ± 253 cc, $p < 0.01$) but no difference in incidence of PPH (6.4% vs. 4.7%, $p = 0.25$). Resolved first-trimester low placentation was also associated with increased tranexamic acid (TXA) administration (11.9% vs. 7.7%, $p = 0.03$), blood transfusion (1.8% vs. 0.4%, $p = 0.04$), and unplanned cesarean delivery (15.3% vs. 9.2%, $p < 0.01$) without differences in the indications for unplanned cesarean delivery. In our multivariable regression, resolved first-trimester low placentation remained associated with TXA administration (adjusted odds ratio [OR], 1.70; 95% confidence interval [CI], 1.07–2.70) and unplanned cesarean delivery (adjusted OR 1.73; 95% CI, 1.12–2.68).

There were no associations with adverse neonatal outcomes or composite maternal outcome.

Conclusion: Resolved first-trimester low placentation is not associated with clinically significant adverse outcomes. However, given changes in unplanned cesarean delivery rate, resolved low placentation may indicate altered uterine physiology. Future research would be valuable to better understand the relationship between resolved low placentation and unplanned cesarean deliveries.

KEYWORDS

first-trimester ultrasound, low-lying placenta, placenta previa, postpartum hemorrhage, transabdominal ultrasound

1 | INTRODUCTION

Low placentation (LP), including placenta covering the internal os and low-lying, affect up to 14% of pregnancies in the first trimester [1]. LP is associated with increased risk of antenatal bleeding, emergency cesarean delivery, and postpartum hemorrhage (PPH) [2]. Placenta previa in particular is associated with preterm birth and increased maternal and fetal morbidity [2, 3]. Even after resolution, LP may pose risks, including antenatal bleeding, PPH, and postpartum IV iron infusion [4–6].

As many as 86% of placentas covering the internal os in the first trimester resolve by the second trimester, with 98.4% resolved by the time of delivery [7]. Current management guidelines suggest that with LP resolution, return to routine prenatal care is recommended [8]. Multiple studies have assessed adverse outcomes after resolution; however, the results and parameters have varied significantly between studies. Some investigations have associated second-trimester LP that resolves by the third trimester with a 2.5- to 5-fold increased risk of PPH delivery [4, 6]. Meanwhile, others have found no relationship between resolved LP and PPH [2].

No prior studies have assessed adverse outcomes associated with a first-trimester resolution of LP. The objective of this investigation was to evaluate delivery outcomes in patients with a transabdominal first-trimester ultrasound diagnosis of LP, which had resolved by the second-trimester detailed ultrasound. We hypothesize that resolution of LP by the second trimester is not associated with adverse delivery outcomes.

2 | MATERIALS AND METHODS

This is a secondary analysis of a retrospective cohort study of singleton pregnancies delivered at a single tertiary care center from January to December 2022, stratified by the presence of LP in the first trimester [5]. Standard recommendations for all patients receiving care at this institution include a first-trimester transabdominal ultrasound for pregnancy dating and early fetal survey between 12+0 weeks and 13+6 weeks. All ultrasonographic evaluations are conducted by accredited fetal sonographers and formally read by maternal-fetal medicine and radiology-trained physicians. In the first-trimester evaluation, LP alone does not necessitate a transvaginal ultrasound. Transvaginal ultrasound is performed for suboptimal imaging, suspected fetal anomalies, or concern for placental pathology such as placenta accreta spectrum or cesarean scar ectopic pregnancy. All patients were identified by querying GE Healthcare Viewpoint 6 Ultrasound Reporting Software for Women's Health.

Patients in the LP group included those with a placenta covering the internal os or low-lying placenta on transabdominal ultrasound evaluation during the first trimester between 12+0 weeks and 13+6 weeks, which subsequently resolved by the second trimester defined as < 28+0 weeks. LP was defined as any portion of the placenta covering the internal cervical os or if the placental edge was located within 20 mm of the internal cervical os. The no-LP group included patients who had both first-trimester and second-trimester ultrasounds without a diagnosis of LP. The no-LP cohort was randomly selected among patients delivering between the study timeline. Representative ultrasound images are shown in Figure 1. Patients were excluded from this study if they had multifetal gestation, prior cesarean delivery, LP persistent beyond the first trimester, or delivery via planned cesarean without a trial of labor.

The primary outcome was quantitative blood loss at delivery by volumetric measurement. Secondary outcomes included the incidence of PPH defined as blood loss ≥1000 mL, unplanned cesarean delivery, tranexamic acid (TXA) administration, use of uterotonics beyond prophylactic pitocin, and composite maternal adverse

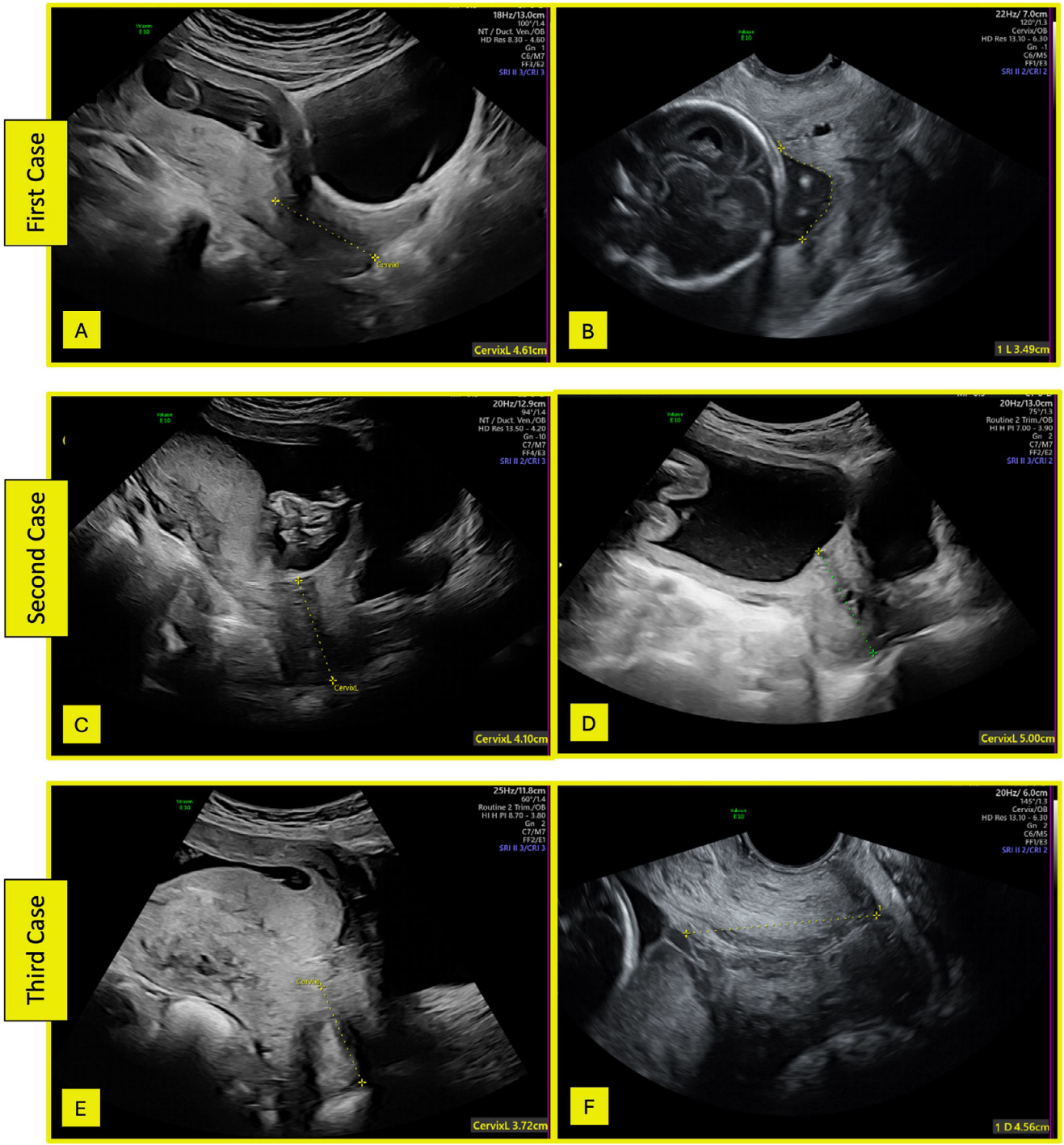

FIGURE 1 Representative cases to highlight diagnostic stratification utilized for study cohorts. First Case (resolved low placentation): placenta covering the internal os at 12+1 weeks (A), then placenta 3.49 cm away from the os at 19+1 weeks (B). Second Case (resolved low placentation): placenta low-lying and close to the internal os at 12+5 weeks (C), then placenta clear of the lower uterine segment at 19+5 weeks (D). Third Case (persistent low placentation at second trimester—excluded from study): placenta covering the internal os at 12+0 weeks (E), then placental edge covering the internal os at 19+3 weeks (F).

outcomes, which included use of atony devices (either JADA system or Bakri balloon), retained products of conception, blood transfusion, peripartum hysterectomy, intensive care unit (ICU) admission, and death. Neonatal outcomes included preterm delivery defined as <37+0 weeks, 5-min Apgar < 7, and neonatal ICU (NICU) admission.

Chi-square and Student's *t*-test, or non-parametric equivalents, were used to determine statistical significance. To determine the strength of association,

TABLE 1 Maternal baseline demographics and characteristics.

	Resolved low placentation ($n = 437$)	No low placentation ($n = 491$)	p value
Maternal age at delivery (years)	32.0 ± 4.9	33.6 ± 4.5	<0.01
Advanced maternal age	137 (31.4)	208 (42.4)	<0.01
Nulliparity	244 (55.8)	216 (44.0)	<0.01
Body mass index at delivery (kg/m^2)	30.1 ± 4.9	31.0 ± 6.2	<0.01
Prior postpartum hemorrhage	12 (2.8)	19 (3.9)	0.34
History of bleeding disorder[a]	21 (4.8)	2 (0.4)	<0.01
Antepartum encounters for bleeding[b]	50 (11.4)	50 (10.2)	0.54
Prior other uterine surgery[c]	61 (14.0)	101 (20.6)	<0.01
In vitro fertilization or assistive reproductive technology	30 (6.9)	40 (8.2)	0.46
Fibroid uterus	34 (7.8)	30 (6.1)	0.32
Uterine anomaly	10 (2.3)	12 (2.4)	0.88
Any hypertensive disorder	91 (20.8)	131 (26.7)	0.04
Any diabetes disorder	60 (13.7)	78 (15.9)	0.36
Gestational age at delivery	39.3 ± 1.3	39.1 ± 1.6	0.07
Neonatal birthweight (g)	3365 ± 476	3319 ± 502	0.15

Note: Categorical outcomes are reported as counts and frequencies. Continuous outcomes are reported as mean ± standard deviation.

[a]History of bleeding disorder includes both inherited (Von Willebrand disease, hemophilia A and B, and factor deficiencies) and acquired (baseline platelet disorders or underlying cirrhosis) diagnoses.

[b]Antepartum encounters for bleeding included emergency room or labor and delivery triage evaluations, or antepartum admission for antenatal vaginal bleeding.

[c]Other uterine surgery includes dilation and curettage/evacuation, diagnostic/operative hysteroscopy, endometrial ablation, or laparoscopic or abdominal myomectomy.

multivariable logistic regression adjusting for advanced maternal age, nulliparity, hypertensive disorder, prior other uterine surgery, and history of bleeding disorder were used and reported as odds ratio (OR). Analysis was performed on STATA IC 15.1, and a p value < 0.05 or 95% confidence interval (CI) not crossing the null was considered significant. This study was approved by the Institutional Review Board prior to data collection.

3 | RESULTS

Of the 3021 first-trimester ultrasound evaluations during the study period, 437 had LP and were included along with 491 no-LP patients as a comparator group (Table 1). Patients with a first-trimester LP were younger, nulliparous, had lower body mass index at delivery, and were less likely to have had prior other uterine surgery or any hypertensive disease (Table 1). A higher number of patients with a history of bleeding disorders was also noted in the LP group (Table 1). There were no other significant differences noted.

Resolved first-trimester LP was associated with a significant increase in quantitative blood loss at delivery (405 ± 369 vs. 331 ± 253 cc, $p < 0.01$) but no difference in incidence of PPH (6.4% vs. 4.7%, $p = 0.25$) (Table 2). Resolved first-trimester LP was also associated with increased TXA administration (11.9% vs. 7.7%, $p = 0.03$), blood transfusion (1.8% vs. 0.4%, $p = 0.04$), and unplanned cesarean delivery (15.3% vs. 9.2%, $p < 0.01$) without differences in the indications for unplanned cesarean delivery (Table 2). After adjustments for nulliparity, advanced maternal age, hypertensive disorder, prior other uterine surgery, and history of bleeding disorder, resolved first-trimester LP remained associated with TXA administration (adjusted OR 1.70; 95% CI, 1.07–2.70; Table 3) and unplanned cesarean delivery (adjusted OR, 1.73; 95% CI, 1.12–2.68; Table 3).

Compared to no-LP group, the LP group had a decreased incidence of NICU admission (3.7% vs. 11.6%, $p < 0.01$) (Table 2), but no association between any other secondary maternal or neonatal outcomes (Table 2).

4 | DISCUSSION

While our study revealed a statistically significant association with resolved first-trimester LP and higher quantitative blood loss, there was no association with clinically significant outcomes such as PPH or composite adverse

TABLE 2 Outcomes comparing patients with resolved low placentation to normal placentation.

	Resolved low placentation ($n = 437$)	No low placentation ($n = 491$)	p value
Quantitative blood loss (cc)	405 ± 369	331 ± 253	<0.01
Postpartum hemorrhage (blood loss >1000 cc)	28 (6.4)	23 (4.7)	0.25
Tranexamic acid administration	52 (11.9)	38 (7.7)	0.03
Additional uterotonics	140 (32.0)	138 (28.1)	0.19
Blood transfusion	8 (1.8)	2 (0.4)	0.04
Composite adverse outcome[a]	14 (3.2)	16 (3.3)	0.96
Unplanned cesarean delivery	67 (15.3)	45 (9.2)	<0.01
Indication for unplanned cesarean	$n = 67$	$n = 45$	0.37
Failed induction of labor	18 (26.9)	6 (14.3)	
Arrest of dilation	15 (23.1)	11 (24.4)	
Arrest of descent	14 (21.5)	9 (20.0)	
Non-reassuring fetal status	20 (29.9)	19 (42.2)	
Preterm delivery (<37+0 weeks)	16 (3.7)	32 (6.5)	0.06
5-min Apgar < 7	6 (1.4)	5 (1.0)	0.62
NICU admission	16 (3.7)	57 (11.6)	<0.01

Note: Categorical outcomes are reported as counts and frequencies. Continuous outcomes are reported as mean ± standard deviation.

Abbreviations: ICU, intensive care unit; NICU, neonatal intensive care unit.

[a]Composite outcome includes use of atony device (Bakri balloon or JADA system), retained products of conception, blood transfusion, peripartum hysterectomy, ICU admission, or death.

TABLE 3 Multivariable logistic regression[a].

	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Tranexamic acid administration	1.61 (1.04–2.50)	1.70 (1.07–2.70)
Unplanned cesarean delivery[b]	1.79 (1.20–2.68)	1.73 (1.12–2.68)

Abbreviations: CI, confidence interval; OR, odds ratio.

[a]Adjusted for advanced maternal age, nulliparity, hypertensive disorder, prior other uterine surgery, and history of bleeding disorder.

[b]Reference was vaginal delivery (spontaneous or operative).

maternal outcome. Notably, the rate of PPH in our cohort was less than in the general obstetric population. The results regarding PPH also vary significantly from the findings of other studies evaluating resolved LP later in gestation. With LP persisting into the second trimester, but resolving prior to delivery, studies reveal a 2.6- to 5.2-fold increased risk of PPH [4, 6]. Combined with our findings, the discrepancy in PPH risk suggests that resolution of LP earlier in pregnancy may reduce the risk of bleeding complications substantially, begging the question of the utility of making a diagnosis of LP in the first trimester.

While resolved first-trimester LP was associated with a higher incidence of blood transfusion, this finding is susceptible to low event rate bias. Additionally, there was an increased use of TXA. It is unclear whether increased utilization of these bleeding interventions is truly a consequence of increased blood loss associated with resolved LP. Overall, these findings are reassuring that in patients with resolved first-trimester LP, the associated risk of complications at the time of delivery is low. These findings may aid in counseling on delivery risk, and avoid unnecessary anxiety, or recommendations for pelvic rest or decreased activity. Based on these data, a diagnosis of resolved first-trimester LP may not warrant changing routine antenatal management.

Another notable association is the increased rate of unplanned cesarean delivery in the LP group, even after adjustment. It remains unclear whether this indicates a possible relationship between resolved LP and changes in intrinsic uterine or placental physiology, or whether other factors belie this association, such as changes in provider decision-making in the setting of resolved LP. Although entirely speculative, some possible alterations in uterine or placental physiology include myometrial contractility or remodeling of lower uterine segment or cervical sites as a result of resolved first-trimester LP.

More research is required to better understand the association between resolved LP and the increased rate of unplanned cesarean deliveries. This may indicate that a higher index of suspicion for labor and delivery complications in this patient population may be appropriate to allow

for more prompt intervention, should they arise. However, conversely, it is important to consider whether this is a result of provider reactions to being aware of a patient's history of resolved LP, and thus whether these interventions are overly invasive and should be avoided.

This study has limitations. First, as a retrospective cohort study, there is potential for human error in manual chart review; however, efforts to mitigate this effect included data points collected as binary or objective characteristics. Second, we are unable to fully account for residual confounding from unmeasured variables, such as placental thickness or degree of extension over the cervical os. Third, since our no-LP cohort was randomly selected, we were unable to match for confounders. Fourth, given this is a secondary analysis, we remain underpowered to adequately assess secondary outcomes such as PPH or blood transfusion. Fifth, given heterogeneity in management of first-trimester LP, we are unable to comment regarding pelvic rest or activity limitations that were given to each individual. Sixth, our cohort was limited to deliveries in 2022, which limits our ability to assess changes in obstetric management. Finally, given that all patient data were sourced from a single academic institution, generalizability may be limited.

This study also has multiple strengths. First, this study was conducted with a relatively large cohort of patients, all of whom received care at a single institution with consistent ultrasound protocols. Second, all patients were offered routine first-trimester transabdominal ultrasound, which decreases the risk of selection bias. Finally, patients with a history of prior cesarean delivery were also excluded to lessen concerns associated with complications related to trial of labor after cesarean, cesarean scar ectopic pregnancy, or placenta accreta spectrum, which may abnormally increase the likelihood of complications associated with LP.

5 | CONCLUSION

First-trimester resolved LP is not associated with clinically significant adverse outcomes. However, given changes in unplanned cesarean delivery rate, resolved LP may indicate altered uterine physiology. Future research would be valuable to better understand the relationship between resolved LP and unplanned cesarean deliveries.

AUTHOR CONTRIBUTIONS

Rachel Feiner: Conceptualization; data curation; investigation; methodology; writing—original and review/editing. **Rachel Wiley**: Conceptualization; investigation; writing review/editing. **Leah Lamale-Smith**: Methodology; supervision; writing—review/editing. **Elizabeth Nicole Teal**: Methodology; supervision; writing—review/editing. **Minhazur Sarker**: Conceptualization; data curation; formal analysis; investigation; methodology; supervision; writing—original and review/editing.

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CONFLICT OF INTEREST STATEMENT

Rachel Wiley consults for Huntleigh Healthcare Ltd, but the work presented here is not related to her work with Huntleigh Healthcare Ltd. All other authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data presented for this study are available upon reasonable request.

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