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ORIGINAL RESEARCH

Perinatal outcomes in pregnancies with very and extremely advanced maternal age: An Italian multicenter retrospective cohort study

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Abstract

Introduction: Pregnancies at very and extremely advanced maternal age (VAMA, 45–49 years and EAMA, ≥50 years) are increasingly common, particularly regarding the influence of assisted reproductive technology (ART), yet their obstetric and perinatal outcomes remain underexplored. This study aimed to investigate maternal and neonatal outcomes in singleton pregnancies among women aged ≥45 years, with a specific focus on ART conception and oocyte source.

Material and Methods: This multicenter retrospective cohort study included women aged ≥45 years with singleton pregnancies delivered ≥22 weeks' gestation between 2016 and 2022 across five Italian academic hospitals. Pregnancies were categorized by mode of conception (spontaneous conception [SC] vs. ART), and ART pregnancies were further stratified by oocyte origin (homologous [ART-HO] vs. heterologous [ART-HE]). Multivariable logistic regression was used to evaluate associations between mode of conception and obstetric outcomes, adjusting for key confounders.

Results: Among 557 included pregnancies, 495 (88.9%) involved women aged 45–49 years, and 62 (11.1%) women aged ≥50. Compared to SC, ART pregnancies were associated with higher adjusted odds of cesarean delivery (aOR 4.20, 95% CI 2.99–4.92; $p < 0.001$) and postpartum hemorrhage (aOR 2.72, 95% CI 1.75–4.23; $p < 0.001$). No significant differences in neonatal outcomes were observed. In the ART subgroup analysis, ART-HE was associated with increased odds of gestational diabetes (aOR 1.97, 95% CI 1.10–3.55; $p = 0.024$) and manual placental removal (aOR 10.45, 95% CI 1.23–88.46; $p = 0.031$) compared to ART-HO.

Conclusions: ART pregnancies in women ≥45 years are associated with increased maternal morbidity, particularly when involving heterologous oocytes. These findings

Abbreviations: ART, assisted reproductive technology; ART-HE, heterologous; ART-HO, homologous; CS, cesarean section; EAMA, extremely advanced maternal age; PPH, postpartum hemorrhage; VAMA, very advanced maternal age.

underscored the need for tailored counseling and multidisciplinary perinatal care in this growing population.

KEYWORDS
advanced maternal age, assisted reproductive technology, cesarean section, gestational diabetes, heterologous oocyte, perinatal outcomes

1 | INTRODUCTION

The frequency of childbearing in women with advanced maternal age above 35 years old has progressively increased worldwide over the last decades.[1] European data reveal a shift in the average age at first childbirth, rising from 28.8 years in 2001 to 31.1 years in 2021, indicating a clear trend toward delayed motherhood.[2] In Italy, the average maternal age at first childbirth is 32.4 years.[3] Several factors contribute to this trend, including societal and professional shifts, as well as advancements in artificial reproductive technologies (ART).[4–7] Such improvements, notably oocyte donation and fertility preservation through oocyte cryopreservation, allow the establishment of pregnancies even in women with very advanced maternal age (VAMA, 45–49 years old) and extremely advanced maternal age (EAMA, 50 years or older).[8–10]

VAMA and EAMA pregnancies have been associated with complications in early gestation, including ectopic pregnancy, miscarriage, and fetal chromosomal abnormalities.[11–14] In addition, increased risks of adverse perinatal outcomes, such as hypertensive disorders of pregnancy, gestational diabetes, placental abnormalities, preterm delivery, maternal and perinatal mortality, and prolonged hospitalization, have been reported.[15–21] Of note, both homologous and heterologous ART have been identified as independent risk factors for adverse pregnancy outcomes when compared to spontaneous conceptions (SC) in the general obstetric population.[22,23] In contrast, little is known about the interplay between advanced age and ART-related risks.[22,24] Yet, VAMA and EAMA pregnancies are often conceived thanks to ART.

Our study aimed to accurately investigate perinatal outcomes among a large cohort of VAMA and EAMA pregnant women and to assess the association of advanced age with adverse pregnancy outcomes according to conception mode and oocyte origin.

2 | MATERIAL AND METHODS

This was a multicentric retrospective observational cohort study including both VAMA (45–49 years old) and EAMA (50 years or older) women with a singleton pregnancy, who delivered at ≥22 weeks' gestation, between January 2016 and January 2022, at five Italian academic maternity centers: Hospital University of Modena (Emilia-Romagna Region), Foundation IRCCS San Gerardo dei Tintori of Monza (Lombardy Region), Vittorio Emanuele III Hospital of Carate Brianza (Lombardy Region), Alessandro Manzoni Hospital of Lecco (Lombardy Region), and Careggi Hospital-University of Florence (Tuscany Region).

Key message

Standardized counseling and multidisciplinary perinatal care pathways are essential to optimize outcomes in women aged ≥45 years.

Data regarding maternal characteristics, mode of conception, pregnancy course, and mode of delivery were collected by reviewing patients' electronic records and encoded as anonymized data into a dedicated Microsoft Excel Spreadsheet. Similarly, postpartum complications as well as neonatal outcomes have been assessed and encoded. ART-conceived pregnancies were further stratified into two sub-groups according to the oocyte origin: homologous [ART-HO] vs. heterologous [ART-HE] to evaluate the potential effects of ART techniques on perinatal outcomes.

2.1 | Statistical analyses

Statistical analyses were conducted using IBM SPSS Statistics version 28 and *open-source software R 4.4*. Distribution of continuous variables was visually assessed. Frequency and proportion were used for categorical variables, whereas mean and standard deviation or median and interquartile range were used for continuous variables not normally distributed, respectively. Fisher's exact or the chi-square test and the Kruskal-Wallis test were employed to determine the difference in frequency distributions among study groups. Medians were compared using the Mann–Whitney U-test. Multivariable logistic regression models were used to estimate associations between outcomes of interest and exposure variables, adjusting for potential confounders as identified by clinical knowledge and published literature. Results were reported as adjusted odds ratios (aORs) with 95% confidence intervals (CIs). All statistical analyses were performed at a significance level of 5%. Figures were generated using GraphPad Prism software.

3 | RESULTS

During the study period, 557 VAMA and EAMA women with a singleton pregnancy were identified, of whom 495 (88.9%) were aged between 45 and 49 years.

Maternal and neonatal characteristics in the overall study population and compared between women with SC and ART conception are described in Table 1.

Women had a median age of 46 years and were mostly Caucasian (88.3%). ART patients were more frequently nulliparous compared to those with SC (86.5% vs. 34.8%, $p<0.001$). No differences were observed in the incidence of gestational diabetes or intrahepatic cholestasis of pregnancy (ICP) between the two study groups, whereas a higher rate of hypertensive disorders of pregnancy, including gestational hypertension and preeclampsia, was observed among ART pregnancies (17.4% vs. 10.9%, $p=0.025$). Preterm birth occurred in 10.2% of deliveries, with similar rates of extremely (<28 weeks), very (28–31 + 6 weeks), and moderate-to-late (32–36 + 6 weeks) preterm birth between groups.

Sixty percent of women delivered by cesarean section (CS), with ART patients showing a higher rate compared to SC (71.1% vs. 40.8%; $p<0.001$), particularly for scheduled prelabor CS (50.6% in ART vs. 25.9% in the SC group; $p<0.001$). Indications for scheduled CS in both SC and ART pregnancies are detailed in Figure 1.

Overall, postpartum hemorrhage (PPH) occurred in 13.7% of women, with those with an ART-conceived pregnancy displaying an almost three-times higher rate than those with SC (17.7% vs. 6.5%, $p<0.001$). No differences were observed regarding neonatal outcomes between the two groups, including umbilical artery pH, Apgar scores, NICU admission, need for respiratory support, and stillbirth.

Multivariable logistic regression analysis confirmed that ART conception was independently associated with a fourfold increased risk of cesarean delivery and a nearly threefold risk of PPH, respectively (Table 2).

Table 3 displays maternal and neonatal characteristics according to the type of ART. An increased risk of gestational diabetes was observed in the ART-HE group compared to ART-HO (27.1% vs. 15%; $p=0.006$). No statistically significant differences were found between the two groups regarding the incidence of ICP, hypertensive disorders of pregnancy, or preterm birth. However, when stratified by gestational age, very preterm birth (28–31 + 6 weeks) occurred exclusively in the ART-HE group (4.2% vs. 0%; $p=0.015$), while no differences were detected for extremely preterm (<28 weeks) or moderate-to-late preterm deliveries (32–36 + 6 weeks).

Regarding the mode of delivery, a higher proportion of CS was recorded in ART-HE pregnancies (74.2% vs. 65%; $p=0.048$), particularly scheduled prelabor CS ($p=0.011$). Among women who delivered vaginally, the rate of manual placenta removal was markedly higher in ART-HE pregnancies (27.7% vs. 3.6%; $p=0.008$). In terms of neonatal outcomes, the only significant difference was a higher rate of 1-minute APGAR scores <7 in the ART-HO group (13.3% vs. 5.1%; $p=0.007$). No significant differences were found for 5-minute Apgar score <7, NICU admission, need for respiratory support, or stillbirths.

Multivariable logistic regression analysis confirmed several findings from the univariate analysis. Compared to ART-HO, ART-HE pregnancies were associated with increased odds of gestational diabetes (aOR 1.97, 95% CI: 1.10–3.55; $p=0.024$) and manual placenta removal (aOR 10.45, 95% CI: 1.23–88.46; $p=0.031$). While CS rates were higher in ART-HE pregnancies in the unadjusted model (OR 1.54, 95% CI: 0.96–2.48), this association did not reach statistical significance after adjustment (aOR 1.43, 95% CI: 0.87–2.34; $p=0.150$) (Table 4).

4 | DISCUSSION

This multicenter retrospective cohort study, conducted across five Italian centers from 2016 to 2022, evaluated maternal and perinatal outcomes among women over 45 years of age who conceived singleton pregnancies either spontaneously or through ART. Our results underscore the high utilization of ART in VAMA and EAMA pregnancies, accounting for 63.9% of the study cohort, and highlight an increased risk of maternal complications associated with ART conceptions compared to SC.

Previous studies have demonstrated that advanced maternal age is an independent risk factor for adverse obstetric outcomes, among which the most consistently reported and clinically significant are hypertensive disorders of pregnancy, gestational diabetes mellitus, placenta previa, increased likelihood of cesarean delivery, and perinatal mortality.[4,25,26]

Also, ART pregnancies, even in younger populations, have shown higher risks for maternal and neonatal complications.[22,26–29] However, few studies have specifically explored the interaction between ART and VAMA. Our study addresses this gap and provides new insights into the additive effects of ART in this high-risk population.

In our adjusted analysis, ART pregnancies among VAMA and EAMA women were associated with a notably increased risk of CS and PPH compared to SC. These findings suggest a substantial maternal burden associated with ART in this population. Although hypertensive disorders appeared more frequent in the crude analysis, this association was attenuated after adjusting for key confounders, highlighting the role of maternal background factors in mediating this risk. The higher cesarean rate observed among ART pregnancies, including those that were planned (41.7%), may reflect both clinical caution in managing precious pregnancies and a higher prevalence of obstetric complications. This is consistent with existing literature suggesting that VAMA and EAMA women often undergo CS due to both medical indications and provider preference.[18,30–32]

Our stratified analysis also revealed that heterologous ART was associated with higher risks of gestational diabetes and manual placental removal compared to ART-HO. The wide confidence interval for placental removal reflects the low event rate in both groups and limits the precision of this estimate, underscoring the need for cautious interpretation of this finding. Although the increased risk of CS in ART-HE compared to ART-HO did not reach statistical significance after adjustment, the trend aligns with previous findings suggesting that ART-HE may be associated with more medicalized obstetric care, including significantly higher rates of CS in oocyte donation pregnancies.[33]

TABLE 1 Comparison of maternal and neonatal characteristics according to mode of conception.

	Overall *n* = (557)	SC (*n* = 201; 34.8%)	ART (*n* = 356; 63.9%)	*p*-Value
Maternal age (median-IQR)	46.0 [45.0–48.0]	46.0 [45.0–46.0]	47.0 [46.0–49.0]	<0.001
Maternal age in categories				<0.001
45–49 years, *n* (%)	495 (88.9)	199 (99)	296 (83)	
≥50 years, *n* (%)	62 (11.1)	2 (1.0)	60 (16.8)	
Caucasian ethnicity, *n* (%)	492 (88.3)	161 (80.1)	331 (93.0)	<0.001
Pre-pregnancy BMI (median-IQR)	23.00 [21.00–26.00]	23.00 [21.00–26.00]	23.00 [21.00–26.00]	0.800
Nulliparity, *n* (%)	378 (67.9)	70 (34.8)	308 (86.5)	<0.001
Previous cesarean section, *n* (%)	62 (11.1)	33 (16.4)	29 (8.1)	0.003
Pre-conceptional diseases, *n* (%)	135 (24)	44 (21.8)	90 (25.5)	0.161
Diabetes mellitus	8 (1.4)	5 (2.5)	3 (0.8)	
Chronic Hypertension	38 (6.8)	11 (5.5)	26 (7.6)	
Gestational diabetes, *n* (%)	123 (22.1)	41 (20.4)	82 (23)	0.271
Hypertensive disorders of pregnancy, *n* (%)[a]	84 (15.1)	22 (10.9)	62 (17.4)	0.025
Intrahepatic cholestasis of pregnancy, *n* (%)	14 (2.5)	3 (1.5)	11 (3.1)	0.193
Fetal malformations, *n* (%)	16 (2.9)	6 (3)	10 (2.8)	0.542
Intrauterine growth restriction, *n* (%)	33 (4.7)	11 (5.5)	22 (6.2)	0.454
Gestational age at delivery, weeks (median-IQR)	39.00 [38.00–40.00]	39.00 [38.00–39.00]	39.00 [38.00–40.00]	0.123
Preterm birth, <37 weeks, *n* (%)	57 (10.2)	21 (10)	36 (10.4)	0.496
Extremely preterm < 28 weeks *n* (%)	4 (0.7)	2 (1)	2 (0.6)	0.456
Very preterm 28–31 + 6 weeks, *n* (%)	17 (3.1)	6 (3)	10 (3.3)	0.583
Moderate to late preterm 32–36 + 6 weeks, *n* (%)	36 (6.5)	13 (6.5)	24 (6.5)	0.564
Spontaneous onset of labor, *n* (%)	125 (22.4)	76 (37.8)	49 (13.8)	<0.001
Induced labor, *n* (%)	173 (31.1)	65 (32)	108 (30.5)	0.345
Mode of delivery, *n* (%)				
Spontaneous vaginal delivery	184 (33.1)	108 (53.7)	76 (21.3)	<0.001
Operative vaginal delivery	38 (6.8)	11 (5.5)	27 (7.6)	0.221
Cesarean section	335 (60.1)	82 (40.8)	253 (71.1)	<0.001
Scheduled cesarean section	232 (41.7)	52 (25.9)	180 (50.6)	<0.001
Urgent cesarean section	103 (18.5)	30 (14.9)	73 (20.5)	0.064
Perineal trauma, *n* (%)	44 (8.1)	16 (8.2)	28 (8)	0.533
Severe (grade 3) laceration, *n* (%)	3 (0.5)	1 (0.5)	2 (0.6)	0.704
Manual removal of placenta, *n* (%)[b]	17 (9.2)	3 (2.9)	14 (18.7)	<0.001
Postpartum blood loss (median-IQR)	450 [300–700]	350 [200–500]	500 [300–800]	<0.001
PPH (>1000 mL), *n* (%)	76 (13.7)	13 (6.5)	63 (17.7)	<0.001
Neonatal weight (median-IQR)	3160 [2832–3500]	3200 [2900–3540]	3140 [2800–3470]	0.075
UA pH <7.0, *n* (%)	6 (1.1)	4 (2)	2 (0.6)	0.121
APGAR <7 at 1st min, *n* (%)	43 (7.7)	15 (7.5)	28 (7.9)	0.499
APGAR <7 at 5th min, *n* (%)	2 (0.4)	-	2 (0.6)	0.412
Neonatal Intensive Care (NICU) Admission, *n* (%)	13 (2.4)	5 (2.6)	8 (2.3)	0.509
Need of Respiratory Support, *n* (%)	67 (12)	20 (10)	47 (13.2)	0.167
Stillbirth, *n* (%)	3 (0.5)	2 (1)	1 (0.3)	0.296

Note: Categorical variables are presented as *n* (%), continuous variables as median (interquartile range).

Abbreviations: ART, assisted reproductive technology; BMI, body mass index; PPH, postpartum hemorrhage; SC, spontaneous conception; UA, umbilical artery; VAMA, very advanced maternal age.

[a]Include gestational hypertension and preeclampsia.

[b]Calculated among women with vaginal delivery.

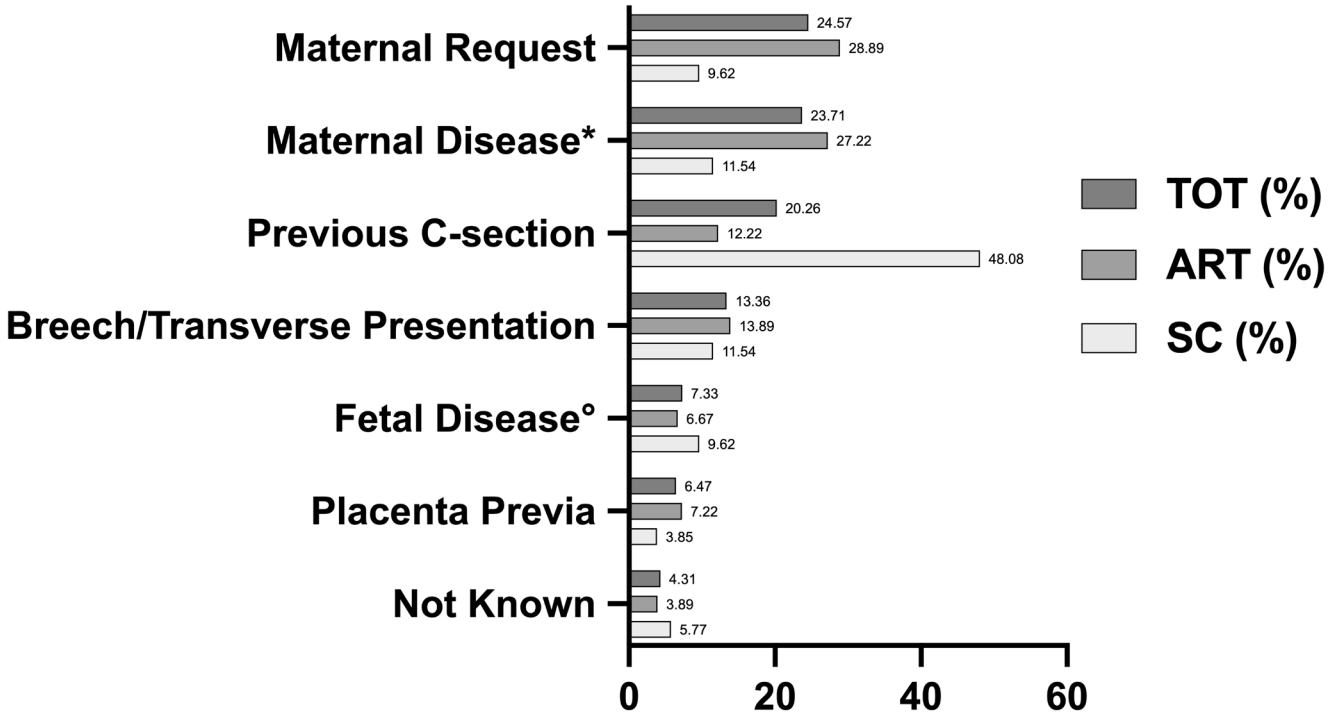

FIGURE 1 Indications for scheduled cesarean section: SC vs. ART. *Preeclampsia, previous myomectomy or other uterine surgery, indications provided by other specialists (orthopedic, ophthalmologic, cardiologic), or associations of multiple risk factors;°Intrauterine growth restriction (IUGR) with abnormal Doppler findings and CTG results Macrosomia.

TABLE 2 Multivariable logistic regression model for perinatal outcomes of interest with SC pregnancies as referent.

		SC vs ART		
Outcomes	**SC**	**Crude OR (95% CI)**	**Adjusted OR (95% CI)**	***p*-Value**
Hypertensive disorders[a]	Ref.	1.99 (1.22–2.25)	1.28 (0.72–2.26)	0.709
Cesarean delivery[b]	Ref.	4.71 (3.18–6.96)	4.20 (2.99–4.92)	<0.001
Postpartum hemorrhage[c]	Ref.	2.92 (2.05–7.17)	2.72 (1.75–4.23)	<0.001

[a]Adjusted for maternal age, ethnicity, and nulliparity.

[b]Adjusted for maternal age, ethnicity, nulliparity, previous Cesarean Section, and hypertensive disorders.

[c]Adjusted for maternal age, ethnicity, nulliparity, previous Cesarean Section, hypertensive disorders, and mode of delivery.

The biological evidence for increased risks with ART, particularly ART-HE, may lie in multiple factors, including advanced maternal age, oocyte quality, and the ART procedures themselves. Several mechanisms have been proposed, including altered endometrial receptivity, immune tolerance disruption, or hormonal environment dysregulation during implantation.[34,35] In addition, ART pregnancies tend to receive closer monitoring and may be more likely to be delivered preemptively, contributing to increased rates of intervention and detection of complications.[36] Differences in embryo handling, freezing techniques, and stimulation protocols may also contribute to the observed variation in outcomes between ART subtypes.[37]

Importantly, while we observed significantly higher maternal morbidity associated with ART pregnancies, neonatal outcomes such as preterm birth and NICU admission did not significantly differ between groups. This finding is consistent with previous literature[22] and suggests that ART in VAMA and EAMA women is primarily associated with maternal rather than neonatal complications.

Given the growing reliance on ART among older women, especially the increasing use of donor oocytes, our findings emphasize the need for comprehensive preconception counseling. Women should be informed about the heightened risks of gestational diabetes, CS, PPH, and potentially rare but severe complications like retained placenta. Care during pregnancy and delivery should be individualized, ideally within a high-risk obstetric center.

Strengths of our study include its multicenter design, with the recruiting centers located in different geographical areas of Italy, and the inclusion of a large cohort of VAMA and EAMA pregnancies, offering novel insights into this high-risk population. It also

TABLE 3 Maternal and neonatal outcomes according to the type of ART.

	ART-HO (33.7%; *n* = 120)	ART-HE (66.3%; *n* = 236)	*p*-Value
Maternal age (median-IQR)	47.00 [46.00–48.00]	47.00 [46.00–49.00]	0.412
Maternal age in categories			
45–49 years, *n* (%)	108 (90)	188 (79.7)	0.009
≥50 years, *n* (%)	12 (10)	48 (20.3)	0.009
Caucasian ethnicity, *n* (%)	110 (91.7)	221 (93.6)	<0.001
Pre-pregnancy BMI (median-IQR)	23.00 [21.00–26.00]	23.00 [21.00–26.00]	0.735
Nulliparity, *n* (%)	97 (80.8)	211 (89.4)	0.040
Previous cesarean section, *n* (%)	6 (5)	23 (9)	0.087
Pre-conceptional diseases, *n* (%)	22 (18.3)	68 (28.5)	0.324
Diabetes mellitus	–	3 (1.3)	
Chronic hypertension	8 (6.7)	18 (7.7)	
Gestational diabetes, *n* (%)	18 (15)	64 (27.1)	0.006
Hypertensive disorders of pregnancy, *n* (%)[a]	23 (19.2)	39 (16.5)	0.315
Intrahepatic cholestasis of pregnancy, *n* (%)	2 (1.7)	9 (3.8)	0.222
Fetal malformation, *n* (%)	2 (1.7)	8 (3.4)	0.287
Intrauterine growth restriction *n* (%)	7 (5.8)	15 (6.4)	0.525
Gestational age at delivery (weeks)	39.00 [37.00–39.14]	38.86 [37.79–39.43]	0.480
Preterm birth (<37 weeks), *n* (%)	11 (9.2)	25 (10.6)	0.413
Extremely preterm < 28 weeks *n* (%)	1 (0.8)	1 (2.1)	0.561
Very preterm 28–31 + 6 weeks, *n* (%)	–	10 (4.2)	0.015
Moderate to late preterm 32–36 + 6 weeks, *n* (%)	10 (8.3)	14 (5.9)	0.260
Spontaneous onset of labor, *n* (%)	20 (16.7)	29 (12.3)	0.166
Induced labor, *n* (%)	46 (38.3)	62 (26.3)	0.014
Mode of delivery, *n* (%)			
Vaginal delivery	28 (23.3)	48 (20.3)	0.301
Operative vaginal delivery	14 (11.7)	13 (5.5)	0.034
Overall cesarean section, *n* (%)	78 (65)	175 (74.2)	0.048
Scheduled cesarean section	50 (41.7)	130 (55.1)	0.011
Urgent cesarean section	28 (23.3)	45 (19.1)	0.210
Perineal trauma, *n* (%)	17 (14.1)	11 (4.6)	0.006
Severe (grade 3) laceration, *n* (%)	2 (1.6)	–	0.143
Manual removal of placenta, *n* (%)[b]	1 (3.6)	13 (27.7)	0.008
Postpartum blood loss (median-IQR)	500 [300–800]	500 [300–800]	0.709
PPH (>1000 ml), *n* (%)	22 (18.3)	41 (17.4)	0.465
Neonatal weight (median-IQR)	3147.00 [2811.25–3560.00]	3140.00 [2790.00–3460.00]	0.190
UA pH <7, *n* (%)	0	2 (0.9)	0.454
APGAR <7 at 1st min, *n* (%)	16 (13.3)	12 (5.1)	0.007
APGAR <7 at 5th min, *n* (%)	–	2 (0.8)	0.439
Neonatal Intensive Care (NICU) Admission, *n* (%)	5 (4.2)	3 (1.3)	0.086
Need of Respiratory Support, *n* (%)	17 (14.2)	30 (12.5)	0.409
Stillbirth, *n* (%)	1 (0.8)	–	0.337

Note: Categoric variables are presented as *n* (%), continuous variables as median (interquartile range).

Abbreviations: ART-H, assisted reproductive technology–heterologous; ART-O, assisted reproductive technology–homologous; PPH, postpartum hemorrhage; UA, umbilical artery; VAMA, very advanced maternal age.

[a]Include gestational hypertension and preeclampsia.

[b]Calculated among women with vaginal delivery.

TABLE 4 Multivariable logistic regression model for perinatal outcomes of interest with ART-HO pregnancies as referent.

		ART-HO VS ART-HE		
Outcomes	**ART-HO**	**Crude OR (95% CI)**	**Adjusted OR (95% CI)**	***p*-value**
Gestational diabetes[a]	Ref.	2.10 (1.18–3.75)	1.97 (1.096–3.55)	0.024
Cesarean section[b]	Ref.	1.54 (0.96–2.48)	1.43 (0.87–2.34)	0.150
Manual removal of placenta[b,c]	Ref.	10.32 (1.27–83.95)	10.45 (1.23–88.46)	0.031

[a]Adjusted for maternal age, ethnicity, and nulliparity.

[b]Adjusted for maternal age, ethnicity, nulliparity, previous cesarean section, and gestational diabetes.

[c]Only among women with vaginal delivery.

uniquely contributes data stratified by ART subtype. However, several limitations warrant consideration. The retrospective nature of the study limited our ability to account for certain factors such as duration and cause of infertility, embryo stage at transfer, or use of frozen versus fresh cycles. Additionally, some outcomes, such as manual placental removal, had few events, resulting in wide confidence intervals and limiting the precision of our estimates.

5 | CONCLUSION

This multicenter cohort study demonstrates that in women aged 45 years and older, conception through ART is associated with increased maternal morbidity compared to SC, particularly in cases involving donor oocytes. ART pregnancies were linked to significantly higher rates of CS and PPH, while the use of donor oocytes was additionally associated with increased risks of gestational diabetes and manual placental removal. Despite similar neonatal outcomes across groups, these findings highlight the importance of comprehensive preconception counseling, individualized risk assessment, and coordinated perinatal care for VAMA women undergoing ART, especially those using donor oocytes. Further studies are warranted to clarify the interplay between maternal age, ART, and obstetric risks in this growing population.

AUTHOR CONTRIBUTIONS

Oumaima Ammar and Maria Teresa Martini were involved in data collection, methodology, analysis, and manuscript drafting. Mariarosaria Di Tommaso, Fabio Facchinetti, and Anna Locatelli contributed to the conceptualization and supervision of the study. Sara Lazzarin and Sara Ornaghi contributed to study design, methodology, and manuscript revision. Anna Luna Tramontano, Cristina Plevani, Viola Seravalli, and Francesca Bonati contributed to data acquisition and critical review of the manuscript. All authors read and approved the final manuscript.

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CONFLICT OF INTEREST STATEMENT

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ETHICS STATEMENT

The present study used retrospective data collection from clinical diaries. At admission, women signed a form permitting the use of their anonymized data for research purposes. Hence, institutional review board approval was not required.

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