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Obstetric outcomes in women of advanced maternal age after assisted reproduction

Anna M. Rubinshtein[1,*], Oleg V. Golyanovskiy[1]

[1] *Department of Obstetrics and Gynecology No1, Shupyk National Healthcare University of Ukraine, 04112 Kyiv, Ukraine*

*Correspondence: anna.rubinshtein@leleka.com.ua (Anna M. Rubinshtein)

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Background: Pregnancy and deliveries resulting from assisted reproductive technology (ART) in women of advanced maternal age (AMA) are reported to be associated with adverse maternal and perinatal outcomes. The aim of the study was to investigate the impact of a combination of AMA and assisted reproduction on obstetric and perinatal outcomes of nulliparous singleton pregnancies. *Methods*: Medical records of 201 live-born singletons, cephalic, non-anomalous nulliparous pregnancies were reviewed retrospectively. The IVF conception (90 AMA women after ART) and spontaneous conception (111 AMA women with spontaneous pregnancy) groups were formed. *Results*: Intrauterine growth restriction, nonreassuring fetal state, operative vaginal delivery, cesarean section, induction of labor, and massive obstetric hemorrhage were more common in AMA patients after ART compared with the spontaneous conception group. The incidence of preeclampsia and nonreassuring fetal status during pregnancy in the IVF conception group was more than 2 times higher than that in the spontaneous conception group. There were no significant differences in spontaneous preterm delivery, Apgar scores, and neonatal morbidity rates between the study groups. *Discussion*: Nulliparous AMA women with pregnancies obtained after ART have inherently higher risks of severe adverse maternal and perinatal outcomes and require careful dynamic monitoring of mother's and fetal conditions followed by prevention and, if possible, correction of disorders during pregnancy and delivery.

Keywords

Nulliparity; Pregnancy complication; Adverse maternal outcomes; Adverse perinatal outcomes

1. Introduction

In recent decades, increasing number of women consider the period of active reproductive age to be most productive for their social activity and career growth; thus, they postpone motherhood for later [1]. The incidence of childbirth among women aged 35+ was 5.1% in the United States, 20% in the United Kingdom, 33.4% in Norway, and 25.9% in Japan [2, 3]. According to the data of the Medical Statistics Center of the Ministry of Health of Ukraine, in 2019, the frequency of births in Ukraine at age 35 years and older was 13.0%; among them, the share of first births was 5.7% and amounted to 7378 cases [4].

The term advanced maternal age (AMA) covers the period from 35 years to menopause [2]. There is no consensus regarding pregnancy and childbirth in women of AMA. These women are more likely to have economic stability; they tend to take better care of their health and maintain a healthy lifestyle. With an increase in age, the number and severity of chronic diseases increases, and the body's adaptive abilities, levels of hormonal secretion, and susceptibility of receptors decrease [5]. Pregnancy during AMA is associated with increased risk of miscarriage, stillbirth, premature birth, macrosomia, intrauterine growth restriction, and preeclampsia [6, 7]. Delivery during AMA is characterized by a higher frequency of cesarean section [2]. In addition, AMA is a risk factor for prolonged and postterm pregnancy, preinduction, and induction of labor [8].

The rationale for this age is a physiological decrease in the number of ovulatory cycles and a general decrease in the fertility of the couple. Therefore, in this case, pregnancy often occurs by assisted reproductive technology (ART) [8, 9]. Shan *et al.* [10], in 2018, have shown that the frequency of ART use clearly increases with age, and this relationship can be graphically represented as a parabola. Of note, the frequency of ART was higher in patients who gave birth for the first time.

Pregnancies resulting from the use of ART have certain features and an increased risk of severe complications [9, 11–13]. According to the results of the analysis by Qin *et al.* [14], singleton pregnancies after ART compared with those after spontaneous conception had a significantly higher risk of gestational hypertension, gestational diabetes, placenta previa, premature placental abruption, and hemorrhage during or after delivery and cesarean section. Furthermore, in the ART pregnancy group, higher risk of preterm birth, intrauterine growth restriction, low birth weight, and higher perinatal mortality were observed.

The aim of this study was to investigate the impact of the combination of AMA and assisted reproduction on obstetric and perinatal outcomes of nulliparous singleton pregnancies.

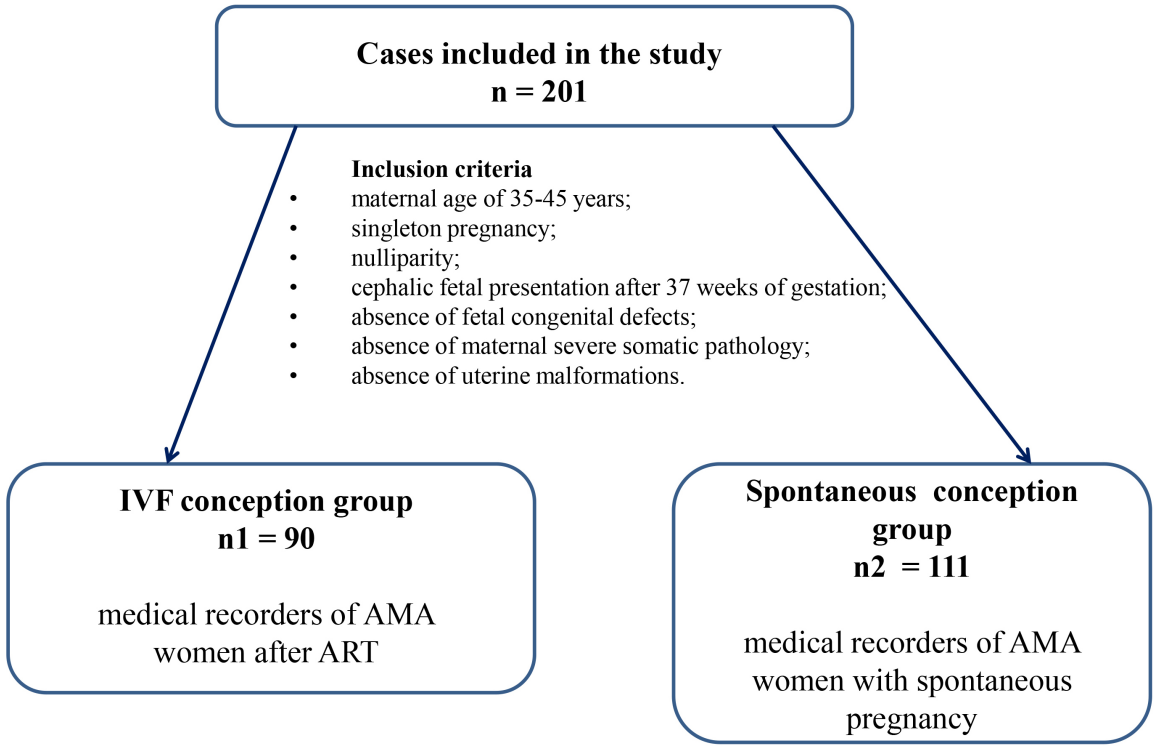

Fig. 1. Study patient inclusion procedure (stufy flow chart).

2. Materials and methods

A retrospective analysis of the prospectively collected database of patients who delivered in 2015–2018 was performed. Patients who met the following criteria were enrolled:

- maternal age of 35–45 years;
- singleton pregnancy;
- nulliparity;
- cephalic fetal presentation after 37 weeks of gestation;
- absence of fetal congenital defects;
- absence of maternal severe somatic pathology;
- absence of uterine malformations.

Egg donor cycles were not included to the study.

Main outcome variables included gestational hypertension, preeclampsia (PE), disease of the placenta accreta spectrum, placenta previa, preterm rupture of membranes, preterm delivery, postterm pregnancy, intrauterine growth restriction (IUGR), nonreassuring fetal state (NRFS), premature placental abruption, delivery of a small or large for gestational age fetus, operative vaginal and cesarean delivery (CS), massive obstetric hemorrhage (MOH), newborns with the Apgar score of 5 and lower in the first minute.

A total of 201 patients met the study criteria, of which 90 AMA women after ART formed the IVF conception group, and 111 AMA women with spontaneous pregnancy were assigned to the spontaneous conception group. Maternal characteristics, perinatal and neonatal results were obtained from the medical recorders (Fig. 1).

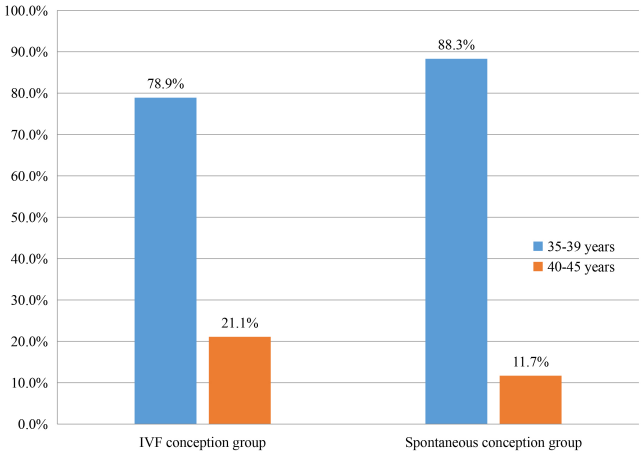

Fig. 2. Age distribution in the study groups.

A descriptive analysis of continuous variables expressed as mean and standard deviations was made. Categorical variables were expressed as percentages. The significance of the difference in proportions was determined using the Student's *t*-test criteria for continuous variables and chi-squared test for categorical variables. To conduct statistical analysis, the odds ratio and 95% confidence interval were calculated. The multivariate analysis was carried out using multiple logistic regression. The level of statistical significance was set at a value of $p < 0.05$.

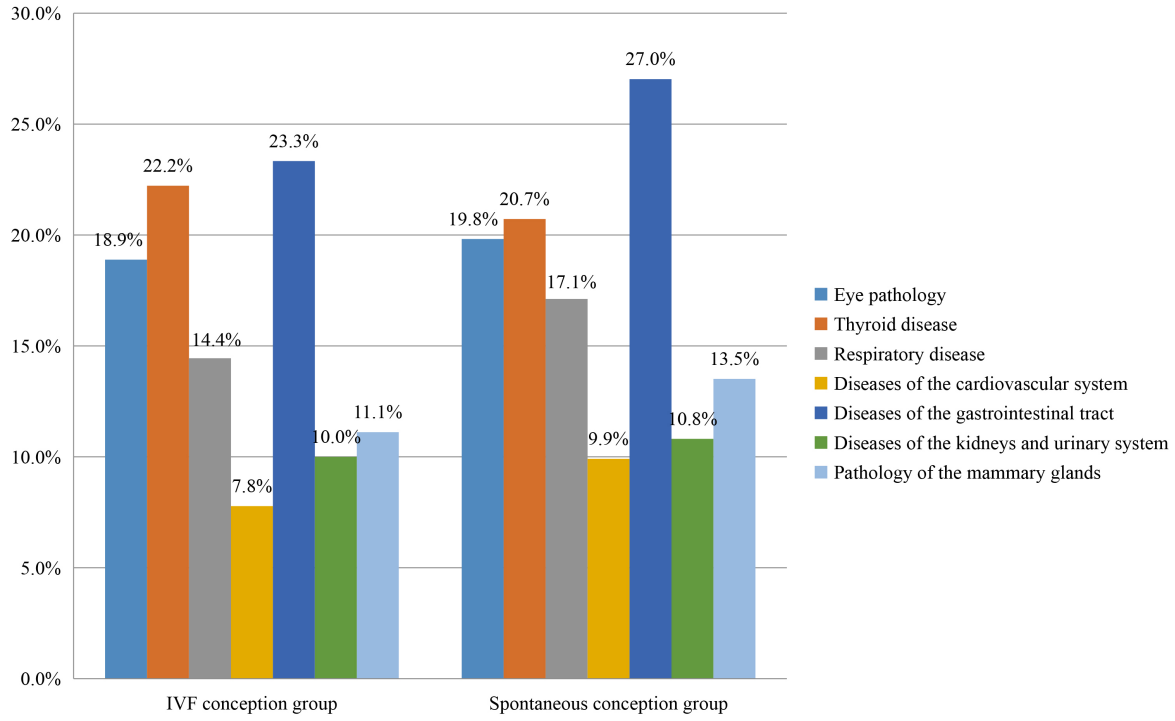

Fig. 3. Extragenital pathology in patients of the study groups.

Table 1. Structure of gynecological morbidity in patients from the study groups.

Gynecological pathology	IVF conception group (n_1 = 90)		Spontaneous conception group (n_2 = 111)		*p*
	Abs. number	%	Abs. number	%	
Ectopic pregnancies	11	12.2	4	3.6	$p = 0.021$*
Miscarriages	17	18.9	12	10.8	$p = 0.105$*
Artificial abortions	10	11.1	18	16.2	$p = 0.3$*
Inflammatory diseases of the pelvic organs	25	27.8	21	18.9	$p = 0.012$*
Functional ovarian cysts	9	10.0	12	10.8	$p = 0.852$*
Uterine fibroids	18	20.0	23	20.7	$p = 0.899$*
Endometriosis	19	21.1	9	8.1	$p = 0.008$*
Polycystic ovary syndrome	9	10	2	1.8	$p = 0.006$*
Uterine polyps	22	24.4	15	13.5	$p = 0.047$*

The *p* value was obtained using the *Chi-squared test.

3. Results

The average age of patients in the IVF conception group was 37.9 ± 0.36; in the spontaneous conception group, it was 36.9 ± 0.19 years ($p > 0.05$); age subgroup distribution is shown in Fig. 2. In the age range of 35–39 years, there were 71 (78.9%) patients in the IVF conception group and 98 (88.3%) patients in the spontaneous conception group; the 40–45-year-old subgroup included 19 (21.1%) women in the IVF conception group and 13 (11.7%) in the spontaneous conception group ($p = 0.0701$).

Fig. 3 shows that there were no significant differences between extragenital diseases in the study groups ($p > 0.05$).

The structure of gynecological pathology in patients from the study groups is shown in Table 1. AMA patients after ART were characterized by a significantly higher incidence of ectopic pregnancies, inflammatory diseases of the pelvic organs (27.8% vs. 18.8% in the spontaneous conception group, $p = 0.012$), uterine polyps (24.4% vs. 13.5% in the spontaneous conception group, $p = 0.047$), endometriosis (21.1% vs. 8.1% in the spontaneous conception group, $p = 0.008$), and polycystic ovary syndrome (10% vs. 1.8% in the spontaneous conception group, $p = 0.006$).

A total of 66.7% of the patients from the IVF conception group had the diagnosis of primary infertility, and 33.3% of the patients had secondary infertility. In terms of the structure, the infertility of tubal-peritoneal genesis occurred in 40% of the cases; male factor occurred in 20%, and infertility of unknown and mixed genesis amounted to 40%.

Table 2 shows the structure of surgical interventions on the pelvic organs and cervix.

Table 2. Structure of surgical interventions on the pelvic organs in patients from the study groups.

Gynecological operations	IVF conception group ($n_1 = 90$)		Spontaneous conception group ($n_2 = 111$)		p
	Abs. number	%	Abs. number	%	
Diagnostic laparoscopy	13	14.4	3	2.7	$p = 0.002$*
Diagnostic hysteroscopy	7	7.8	0	0	$p = 0.003$*
Polypectomy	22	24.4	13	11.7	$p = 0.018$*
Ovarian surgery	11	12.2	14	12.6	$p = 0.934$*
Tubectomy	15	16.7	7	6.3	$p = 0.019$*
Conservative myomectomy	14	15.6	17	15.3	$p = 0.963$*

The p value was obtained using the *Chi-squared test.

Table 3. Structure of pregnancy complications in the study group.

Pregnancy complications	IVF conception group ($n_1 = 90$)		Spontaneous conception group ($n_2 = 111$)		p
	Abs. number	%	Abs. number	%	
Gestational hypertension	4	4.4%	3	2.7%	$p = 0.503$*
Preeclampsia	8	8.9%	4	3.6%	$p = 0.116$*
Severe preeclampsia	2	2.2%	1	0.9%	$p = 0.442$*
IUGR	13	14.4%	5	4.5%	$p = 0.014$*
NRFS	7	7.7	4	3.6%	$p = 0.196$*
Anemia	32	35.6%	46	41.4%	$p = 0.395$*
Hypothyroidism, drug correction	11	12.2%	12	10.8%	$p = 0.755$*
Gestational diabetes mellitus	14	15.6%	17	15.3%	$p = 0.963$*
Intrahepatic cholestasis	15	16.7%	7	6.3%	$p = 0.019$*
Threat of miscarriage	37	41.1%	45	40.5%	$p = 0.935$*
Cervical incompetence	8	8.9%	6	5.4%	$p = 0.229$*
Threat of premature birth	20	22.2%	25	22.5%	$p = 0.96$*
Upper respiratory tract infections	11	12.2%	15	13.5%	$p = 0.786$*
Infections of the urinary system	5	5.6%	9	8.1%	$p = 0.627$*

The p value was obtained using the *Chi-squared test.

Taking into account the peculiarities of preparation for ART cycles, it is clear that there is higher frequency of diagnostic hystero- and laparoscopies in the IVF conception group (7.8% vs. 0%, $p = 0.003$ and 14.4% vs. 2.7%, $p = 0.002$). Patients from the IVF conception group were significantly more likely to undergo polypectomy and surgery for ectopic pregnancy.

According to the data shown in Table 3, in the IVF conception group, gestational hypertension, preeclampsia, and NRFS were observed relatively more often ($p > 0.05$). The incidence of preeclampsia and NRFS in AMA patients after ART was more than 2 times higher than that in patients in the spontaneous conception group. Intrauterine growth restriction was diagnosed in 14.4% of the cases in the IVF conception group and in 4.5% of the cases in the spontaneous conception group ($p = 0.014$).

Intrahepatic cholestasis was diagnosed significantly more often in the IVF conception group (16.7% vs. 6.3%, $p = 0.019$).

The threat of preterm labor and complicated pregnancy was in more than 20% of the patients in both study groups. In 8.9% of the patients in the IVF conception group and in 5.4% of the spontaneous conception group, cervical shortening of less than 25 mm was diagnosed, which required the installation of an obstetric pessary and subsequent therapy with micronized progesterone. In the second and third trimesters (up to 36 weeks), micronized progesterone in different doses (200–800 mg) was received by 42.3% of the patients in the IVF conception group and by 38.7% of the patients in the control ($p > 0.05$).

The incidence of preterm birth did not differ significantly and amounted to 16.2% in the IVF conception group and 14.4% in the control group. Delivery during 37 + 0–40 + 6 week terms occurred less frequently ($p = 0.107$) in the IVF conception group (in 55.6% of the cases), compared to 66.7% in the spontaneous conception group. The tendency for post-term pregnancy was clearly observed in the group of AMA patients after ART; thus, the odds ratio of delivery after 41 + 0 weeks, including induced, was 2.07 (95% CI 1.06–4.05, $p = 0.03$). Patients in the IVF conception group were twice as likely to have preinduction/induction of labor compared to patients in the spontaneous conception group (OR = 2.13; 95% CI 1.06–4.25, $p = 0.033$). The frequency of unsuccessful attempts to induce labor was slightly higher in the IVF conception group, i.e., 6.7% vs. 2.7% ($p = 0.174$).

The frequency of vaginal delivery in the group of AMA patients after ART was 54.5%, and it was significantly lower than that in the group of AMA patients with spontaneous pregnancy, i.e., 73% ($p = 0.0063$). The frequency of phys-

Table 4. Indications for cesarean section.

Indication	IVF conception group ($n_1 = 90$)		Spontaneous conception group ($n_2 = 111$)		p
	Abs. number	%	Abs. number	%	
Clinical narrow pelvis	8	8.9%	7	6.3%	$p > 0.05$*
Weakness of labor	8	8.9%	8	7.2%	$p > 0.05$*
- primary	4	4.4%	5	4.5%	$p > 0.05$*
- secondary	4	4.4%	3	2.7%	$p > 0.05$*
- NRFS	15	15.6%	11	9.9%	$p > 0.05$*
- during pregnancy	5	5.6%	4	3.6%	$p > 0.05$*
- during the first stage of labor	10	11.1%	7	6.3%	$p > 0.05$*
Unsuccessful induction of labor	6	6.7%	3	2.7%	$p > 0.05$*
Premature placental abruption	4	4.4%	1	0.9%	$p > 0.05$*

The p value was obtained using the *Chi-squared test.

iological vaginal delivery was 35.6% in the IVF conception group and 60.4% in the spontaneous conception group. AMA pregnant women after ART were almost three times less likely to have a physiological vaginal delivery than pregnant women of the same age with spontaneous pregnancy (OR = 2.76; 95% CI 1.5526–4.9061; $p = 0.0005$).

The average blood loss was significantly higher ($p = 0.0004$) in the IVF conception group and was 600.3 ± 35.8 mL vs. 449.6 ± 21.3 mL in the spontaneous conception group. The average blood loss during vaginal delivery was also higher ($p = 0.0046$) in the IVF conception group, i.e., 367.0 ± 10.9 mL in the IVF conception group and 327.8 ± 8.1 mL in the spontaneous conception group. During the cesarean section, blood loss in the study groups was 892 ± 49.5 mL and 757.7 ± 15.6 mL ($p = 0.012$) in the main and spontaneous conception groups, respectively.

Massive obstetric hemorrhage (MOH) rate was higher in the IVF conception group and amounted to 5.6% vs. 0.9% in the spontaneous conception group ($p = 0.053$). Probability to develop MOH in AMA patients after ART was 6.5 times higher (95% CI 0.74–56.42; $p = 0.09$).

In the IVF conception group, NRFS was diagnosed significantly more often in 26.7% of cases, in the spontaneous conception group—in 15.3% ($p = 0.019$). During the first and second stages of labor, the NRFS distribution was approximately the same.

The frequency of instrumental vaginal delivery (IVD) was almost 2 times higher in the IVF conception group and amounted to 13.3% vs. 7.2% in the spontaneous conception group; however, a significant difference between these indicators was not observed ($p = 0.15$). Indications for IVD in the study groups were distributed as follows, i.e., fetal distress in the second period of delivery: 11.1% in the IVF conception group and 4.5% in the spontaneous conception group; weakness during the pushing stage: 2.2% in the IVF conception group vs. 2.7% in the control group.

A total of 45.5% of patients in the IVF conception group delivered by cesarean section; operative abdominal delivery in the spontaneous conception group was performed in 27.0%. Thus, pregnant AMA women after ART had more than 2 times higher risk of cesarean section than AMA patients with spontaneous pregnancy (OR = 2.26; 95% CI 1.253–4.074; $p = 0.0067$).

According to Table 4, the structure of indications for cesarean section in the study groups was relatively homogeneous.

One of the most common complications of the postpartum period was anemia. The average hemoglobin levels during the postpartum period in the study groups had no significant differences ($p = 0.2$) and were 108.8 ± 1.9 g/L in the IVF conception group and 105.9 ± 1.4 g/L in the spontaneous conception group. During the postpartum period, the diagnosis of anemia was established in 44.4% of patients from the IVF conception group; while in the spontaneous conception group, anemia was observed in 39.7% of the patients.

Complications from the side of the postoperative wound (seroma, hemaroma) after cesarean section were observed relatively rarely, i.e., in 2% of the patients from both groups. Inflammation and divergence of perineal sutures were observed in 3.3% of the patients in the IVF conception group and in 4.5% of the patients from the spontaneous conception group.

The average weight of full-term infants was 3447 ± 63.3 g in the IVF conception group and 3524.6 ± 77.2 g in the spontaneous conception group ($p > 0.05$); the average body length was 52.4 ± 0.45 cm in the IVF conception group and 54.1 ± 0.59 cm in the spontaneous conception group ($p > 0.05$). However, in the IVF conception group, children with a body weight of 4000 g and more were born more often; the share of heavy newborns in the IVF conception group was 16.7%, in the control group—13.5% ($p > 0.05$).

The average scores of newborns on the Apgar scale did not differ significantly ($p > 0.05$) and were, at the first minute, 7.64 ± 0.12 in the IVF conception group vs. 7.85 ± 0.18 in the control; at the fifth minute, the scores were 8.75 ± 0.15 in the IVF conception group vs. 8.56 ± 0.14 in the control group. A total of 3.3% of newborns in the IVF conception group and 1.8% in the spontaneous conception group had a score of 5 points or lower on the Apgar scale at the first minute of life ($p > 0.05$). Medical care (tactile stimulation,

airway sanitation, oxygen support, and pain relief) immediately after birth was needed for 15.6% of infants in the IVF conception group and for 10.8% of infants in the spontaneous conception group ($p > 0.05$).

The main complications of the intra- and neonatal period were neonatal jaundice (16.7% in the IVF conception group and 13.5% in the spontaneous conception group, $p > 0.05$), moderate asphyxia at birth (7.8% in the IVF conception group and 5.4% in the spontaneous conception group, $p > 0.05$), cephalohematoma (3.3% in the IVF conception group and 6.3% in the spontaneous conception group, $p > 0.05$), and intrauterine fetal infection (3.3% in the IVF conception group and 3.6% in the spontaneous conception group, $p > 0.05$). Respiratory distress syndrome was manifested in 4.4% of premature infants in the IVF conception group and in 2.7% of premature infants in the spontaneous conception group ($p > 0.05$).

The multivariate logistic regression analysis was done to check the reliability of the difference, identify and assess additional risk factors for complications during pregnancy and labor. We assessed the impact of the following factors: age 40–45 years, endometriosis, polycystic ovary syndrome (PCOS), and uterine polyps; on the frequency of such complications of pregnancy and labor as PE, IUGR, IHH, pathological delivery, delivery in terms of 41–42 weeks, induction of labor, CS, NRFS, MOH.

The results obtained in the IVF conception group are presented in Table 5. Thus, the factor of age 40 years and older significantly increased the likelihood of developing PE (OR = 9.691; 95% CI 2.136–54.56, $p = 0.0047$), IUGR (OR = 7.48; 95% CI 2.051–29.45, $p = 0.0026$), IHH (OR = 5.158; 95% CI 1.525–17.69, $p = 0.0078$), delivery in terms 41–42 weeks (OR = 2.879; 95% CI 0.9605–8.972, $p = 0.0607$), induction of labor (OR = 5.187; 95% CI 1.732–17.16, $p = 0.0044$), CS (OR = 3.407; 95% CI 1.120–11.35, $p = 0.0355$), and NRFS (OR = 5.210; 95% CI 1.746–16.26, $p = 0.0034$). Endometriosis increased the likelihood of CS (OR = 3.291; 95% CI 1.103–10.53, $p = 0.0364$); the presence of endometrial polyps and, accordingly, a history of hysteroresectoscopy increased the likelihood of MOH (OR = 5.579; 95% CI 1.403–24.64, $p = 0.0160$); PCOS increased the likelihood of PE (OR = 6.935; 95% CI 1.087–43.63, $p = 0.0336$), IUGR (OR = 4.298; 95% CI 0.7033–23.66, $p = 0.0940$), delivery in terms of 41–42 weeks (OR = 4.909; 95 % CI 1.119–26.36, $p = 0.0420$), pathological delivery (OR = 6.825; 95% CI 1.062–134.5, $p = 0.0864$), C-section (OR = 6.433; 95% CI 1.356–47.11, $p = 0.0313$).

In the spontaneous conception group, the age factor 40 years and older significantly increased the likelihood of developing PE (OR = 9.229; 95% CI 0.9900–91.28, $p = 0.0394$), IUGR (OR = 9.343; 95% CI 0.9686–96.31, $p = 0.0424$), delivery in terms 41–42 weeks (OR = 4.188; 95% CI 1.186–14.61, $p = 0.0230$), induction of labor (OR = 5.018; 95% CI 1.424–17.52, $p = 0.0104$), pathological delivery (OR = 4.020; 95% CI 1.189–15.99, $p = 0.0316$), CS (OR = 4.327; 95% CI 1.275–15.21, $p = 0.0185$), NRFS (OR = 5.599; 95% CI 1.429–21.14, $p = 0.0107$). Endometriosis significantly increased the likelihood of delivery in terms of 41–42 weeks (OR = 3.927; 95% CI 0.8536–17.21, $p = 0.0671$). PCOS significantly increased the likelihood of developing PE (OR = 59.11; 95% CI 1.631–2630, $p = 0.0165$), and IUGR (OR = 41.45; 95% CI 1.051–1764, $p = 0.0322$), but a small number (2 women) of PCOS cases should be noted in the group (Table 6).

Thus, during the multivariate logistic regression analysis, it was shown that the age of 40 years and older is authentically associated with increased pregnancy and labor complications, and accordingly forms confounding effects on the pregnancy outcomes. An additional assessment of the total effect of PCOS, endometriosis, and uterine polyps as predictors of complications is also considered.

4. Discussion

AMA patients with infertility were characterized by significantly higher levels of different gynecological pathology; we believe that the abovementioned reason was the cause of infertility. Taking into account the peculiarities of ART cycles, it was clear that patients from the IVF conception group had a significantly greater number of surgical abdominal and intrauterine interventions, which in turn could increase the risk of placenta accreta spectrum diseases.

Based on the results of a retrospective analysis, a specific complication of pregnancy in AMA patients after ART was the development of intrahepatic cholestasis. We believe that the risk factor for the development of this complication is hormonal stimulation and long-term high-dose hormonal drug support.

According to the high frequencies of intrauterine growth restriction, preeclampsia, and NRFS during pregnancy, AMA patients after ART require more thorough and frequent diagnostic procedures.

Both study groups were equally characterized by the high frequency of the threat of termination of pregnancy and preterm delivery. The increased risks of preterm birth in both groups were probably associated with age-related changes in progesterone synthesis and peculiarities of the functioning of the receptors. At the same time, AMA patients after ART had more than two times higher chances of having preinduction/induction of labor at 41–42 weeks of gestation to prevent prolonged pregnancy.

According to the study results, AMA women after ART are at the high risk of having an urgent C-section. Taking into account the higher blood loss and more frequent MOH, we believe that these patients must be administered uterotonic and hemostatic drugs (carbetocin 100 μg intravenously and tranexamic acid 1 g intravenously) immediately after cord clamping to prevent these complications.

It should also be noted that the risks of complications significantly increase in the subgroup of patients aged 40–45 years. Regardless of the presence or absence of other risk factors, these patients need particularly careful monitoring of their condition at all stages of pregnancy and labor. We also

Table 5. Multivariate logistic regression analysis in the IVF conception group.

Variable	Odds ratios	95% CI	p
Dependent variable		Preeclampsia	
Intercept	0.03855	0.008102–0.1244	$p < 0.0001$
Age 40–45 years	7.942	1.918–37.18	$p = 0.0047$
Endometriosis	3.281	0.6562–16.38	$p = 0.1030$
Uterine polyps	0.7844	0.09152–4.395	$p = 0.8072$
PCOS	6.935	1.087–43.63	$p = 0.0033$
Dependent variable		IUGR	
Intercept	0.06819	0.01919–0.1838	$p < 0.0001$
Age 40–45 years	7.483	2.051–29.45	$p = 0.0026$
Endometriosis	1.295	0.2362–5.819	$p = 0.7445$
Uterine polyps	0.9778	0.1721–4.406	$p = 0.9777$
PCOS	4.298	0.7033–23.66	$p = 0.0940$
Dependent variable		IHH	
Intercept	0.09810	0.03299–0.2383	$p < 0.0001$
Age 40–45 years	5.158	1.525–17.69	$p = 0.0078$
Endometriosis	1.620	0.3698–6.259	$p = 0.4941$
Uterine polyps	1.343	0.3120–5.068	$p = 0.6714$
PCOS	1.573	0.1991–8.466	$p = 0.6208$
Dependent variable		Delivery in terms 41–42 weeks	
Intercept	0.2671	0.1233–0.5301	$p = 0.0003$
Age 40–45 years	2.879	0.9605–8.972	$p = 0.0607$
Endometriosis	2.300	0.7620–7.038	$p = 0.1379$
Uterine polyps	2.104	0.7249–6.189	$p = 0.1699$
PCOS	4.909	1.119–26.36	$p = 0.0420$
Dependent variable of labor		Induction	
Intercept	0.2998	0.1414–0.5877	$p = 0.0008$
Age 40–45 years	5.187	1.732–17.16	$p = 0.0044$
Endometriosis	1.175	0.3633–3.620	$p = 0.7802$
Uterine polyps	1.909	0.6528–5.606	$p = 0.2340$
PCOS	2.662	0.5910–12.57	$p = 0.1979$
Dependent variable		Pathological delivery	
Intercept	0.7343	0.3795–1.388	$p < 0.0001$
Age 40–45 years	6.554	1.589–45.02	$p = 0.4186$
Endometriosis	8.193	2.002–56.17	$p = 0.2451$
Uterine polyps	1.824	0.6079–5.862	$p = 0.9227$
PCOS	6.825	1.062–134.5	$p = 0.0864$
Dependent variable		C-section	
Intercept	0.3739	0.1828–0.7177	$p = 0.0045$
Age 40–45 years	3.407	1.120–11.35	$p = 0.0355$
Endometriosis	3.291	1.103–10.53	$p = 0.0364$
Uterine polyps	1.391	0.4786–4.045	$p = 0.5411$
PCOS	6.433	1.356–47.11	$p = 0.0313$
Dependent variable		NRFS	
Intercept	0.2460	0.1109–0.4969	$p = 0.0002$
Age 40–45 years	5.210	1.746–16.26	$p = 0.0034$
Endometriosis	1.297	0.3695–4.206	$p = 0.6712$
Uterine polyps	0.8122	0.2236–2.602	$p = 0.7354$
PCOS	0.7340	0.09625–3.652	$p = 0.7277$
Dependent variable		MOH	
Intercept	0.06979	0.01811–0.1947	$p < 0.0001$
Age 40–45 years	1.050	0.1389–5.289	$p = 0.9559$
Endometriosis	0.5572	0.02811–3.762	$p = 0.6043$
Uterine polyps	5.579	1.403–24.64	$p = 0.0160$
PCOS	0.9971	0.04725–7.571	$p = 0.9980$

Table 6. Multivariate logistic regression analysis in the spontaneous conception group.

Variable	Odds ratios	95% CI	p
Dependent variable		Preeclampsia	
Intercept	0.01619	0.002035–0.06123	$p < 0.0001$
Age 40–45 years	9.229	0.9900–91.28	$p = 0.0394$
Endometriosis	4.833	0.2015–60.29	$p = 0.2308$
Uterine polyps	1.092	0.03066–12.75	$p = 0.9505$
PCOS	59.11	1.631–2630	$p = 0.0165$
Dependent variable		IUGR	
Intercept	0.01058	0.001018–0.04748	$p < 0.0001$
Age 40–45 years	9.343	0.9686–96.31	$p = 0.0424$
Endometriosis	7.369	0.2875–115.6	$p = 0.1488$
Uterine polyps	5.201	0.4397–57.34	$p = 0.1576$
PCOS	41.45	1.051–1764	$p = 0.0322$
Dependent variable		IHH	
Intercept	0.03836	0.01018–0.1015	$p < 0.0001$
Age 40–45 years	7.161	1.258–37.87	$p = 0.0189$
Endometriosis	2.202	0.1014–18.61	$p = 0.5146$
Uterine polyps	1.112	0.05328–8.386	$p = 0.9279$
Dependent variable		Delivery in terms 41–42 weeks	
Intercept	0.1750	0.09026–0.3116	$p < 0.0001$
Age 40–45 years	4.188	1.186–14.61	$p = 0.0230$
Endometriosis	3.927	0.8536–17.21	$p = 0.0671$
Uterine polyps	1.447	0.3374–5.194	$p = 0.5878$
PCOS	4.751	0.1742–128.4	$p = 0.2883$
Dependent variable of labor		Induction	
Intercept	0.1548	0.07739–0.2814	$p < 0.0001$
Age 40–45 years	5.018	1.424–17.52	$p = 0.0104$
Endometriosis	1.454	0.1933–7.213	$p = 0.6713$
Uterine polyps	1.570	0.3599–5.753	$p = 0.5145$
PCOS	5.158	0.1877–140.2	$p = 0.2652$
Dependent variable		Pathological delivery	
Intercept	0.4646	0.2838–0.7399	$p = 0.0016$
Age 40–45 years	4.020	1.189–15.99	$p = 0.0316$
Endometriosis	2.361	0.5671–10.39	$p = 0.2336$
Uterine polyps	2.726	0.8670–9.105	$p = 0.0893$
PCOS	1.304	0.04591–36.04	$p = 0.8588$
Dependent variable		C-section	
Intercept	0.2203	0.1198–0.3786	$p < 0.0001$
Age 40–45 years	4.327	1.275–15.21	$p = 0.0185$
Endometriosis	3.109	0.6828–13.40	$p = 0.1253$
Uterine polyps	2.291	0.6550–7.563	$p = 0.1772$
PCOS	2.998	0.1073–82.13	$p = 0.4585$
Dependent variable		NRFS	
Intercept	0.09425	0.03985–0.1908	$p < 0.0001$
Age 40–45 years	5.599	1.429–21.14	$p = 0.0107$
Endometriosis	0.9600	0.04702–6.644	$p = 0.9717$
Uterine polyps	2.900	0.6632–11.29	$p = 0.1322$

consider the option of an elective CS in the terms of 39–40 weeks for nulliparous women aged 40–45 years with a combination of the abovementioned predictors or other pregnancy complications, especially with IVF conception.

5. Conclusions

Nulliparous AMA women with pregnancy after ART have inherently higher risks of severe adverse maternal and perinatal outcomes and require careful dynamic monitoring of the mother's and fetal conditions, prevention and, if possible, correction of disorders at the initial stages during pregnancy and delivery. The risks of pregnancy and labor complications increase significantly with the patients' age.

Author contributions

AMR and OVG conceived and designed the study. AMR undertook collection, cleaning, analysis and interpretation of the data, wrote the earlier manuscript drafts, and prepared tables and figures. OVG revised subsequent manuscript drafts, reviewed records, provided expertise throughout the study, and contributed to the final approval of the completed article. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The study was approved by the ethics committee of the P.L. Shupik National Medical Academy of postgraduate education (Protocol number 7, date of approval: 07.10.2019). Our institution's ethics committee does not require informed consent for retrospective study. Therefore, consent was not obtained in accordance with institutional guidelines.

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Conflict of interest

The authors declare no conflict of interest.

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