

# Obstetric and neonatal outcomes in women aged 40 years or older after in vitro fertilization

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## Summary

**Purpose of investigation:** The aim of this study was to determine the rate of complications in pregnancy and during delivery, as well as neonatal outcomes, in women who underwent in vitro fertilization (IVF) and who are 40 years of age or older. **Materials and Methods:** This was a prospective study. The study group consisted of 29 women who underwent IVF. The control group consisted of 32 women who had a spontaneous pregnancy. **Results:** Pregnancy complications occurred in 86.21% of women in the study group, and in 46.87% of women in the control group. The proportion of cesarean sections (CS) was 84.62% in the study group, and 21.87% in the control group. Birth weight < 1,500 grams and < 2,500 grams was present in 17.16% and 22.86% of newborns in the study group, respectively. In the control group, birth weight < 1,500 grams and < 2,500 grams was present in 5.55% and 8.33% of newborns, respectively. Neonatal intensive care unit admissions included 22.86% newborns from the study group and 8.33% from the control group. **Conclusion:** Pregnancy, delivery, and neonatal complications were more frequent in the study (IVF) group.

**Key words:** In vitro fertilization; Pregnancy; Delivery; Newborn.

## Introduction

The advancement of various assisted reproductive technology (ART) methods in the past 30 years, as well as availability of oocyte and embryo donation, has enabled women, in their fifth and sixth decades of life, to become pregnant and give birth. Approximately 19% of women undergoing an ART procedure are over the age of 40 years [1]. Female fertility declines with age, especially after 40 years. This may partially be due to a decrease in ovarian reserve and endometrial receptivity, but also an increased number of aneuploidies, which increases the risk of miscarriage. The success rate of in vitro fertilization (IVF) remains favourable for women until the end of the 43<sup>rd</sup> year of life. The success rate for IVF at the age of 44 years is 3% live births per cycle, which further declines at the age of 45 years to 1% live births [2]. Women, 44 years of age or older, should be advised to undergo IVF with donated oocytes due to low success rates using their own oocytes [3]. Multiple studies have demonstrated significantly higher proportions of maternal morbidity, delivery complications, and neonatal morbidity in older women undergoing IVF compared to those who are younger [4-8].

## Objectives

The aim of this study was to determine the rate of pregnancy and delivery complications, as well as neonatal outcomes, in 40-year-old or older women, undergoing IVF with or without oocyte/embryo donation, compared to

women between the ages of 35 to 39 years, who had a spontaneous pregnancy.

## Materials and Methods

A prospective study was conducted at the Obstetrics and Gynecology Hospital "Narodni Front" in Belgrade, from 2009 to 2011. The study group consisted of 29 women between the ages of 40 and 54 years, who underwent IVF and conceived, with or without oocyte/embryo donation. Publicly funded healthcare provides coverage of IVF for women until the age of 40 years, and for this reason, all of the study participants underwent IVF at various other centres. After the age of 40 years, IVF procedures are performed at privately funded institutions. Meanwhile, donation of oocytes/embryos is available in other European countries. All women in the study group received prenatal care at the present clinic, where they also delivered.

The control group consisted of 32 women between the ages of 35 and 39 years, who spontaneously conceived during a normal menstrual cycle. All women in the control group received prenatal care at the present hospital, where they also delivered. Due to low rates of spontaneous pregnancy after the age of 40 years and this two-year study period, the control group consisted of women aged 35 to 39 years.

The proportion of study group women according to the IVF centre was as follows: 27.0%, aged 45-54 years, from the Specialized Hospital "Belgrade" (n=8), 56.82%, aged 40-50 years, from the Prenatal Sanatorium (n=17), and 14.38%, aged 40-45 years, from other centres (n=4).

Based on the method of conception, the study group was divided into three subgroups. The first subgroup consisted of women who underwent IVF-ICSI (intracytoplasmic sperm injection) with own

Table 1. — Age category and conception method in study group women.

Conception method	Age category							
	40-44 years		45-49 years		50-54 years		Total	
	N	%	N	%	N	%	N	%
IVF-ICSI (own oocytes)	6	20.68	0	0	0	0	6	20.66
IVF- donated oocytes	8	27.58	11	37.93	1	3.44	20	68.96
Embryo donation	0	0	0	0	3	10.34	3	10.34
TOTAL	14	48.27	11	37.93	4	13.79	29	100.0

IVF – in vitro fertilization; ICSI – intracytoplasmic sperm injection.

Table 2. — Type of pregnancy and age category in study and control groups.

Age category (years) Type of pregnancy	Study group						Total		Control group	
	40-44		45-49		50-54				35-39	
	N	%	N	%	N	%	N	%	N	%
Singleton	13	44.82	4	13.79	3	10.34	20	68.97	30	93.75
Twins	1	3.45	7	24.14	0	0	8	27.59	2	6.25
Triplets	0	0	0	0	1	3.45	1	3.45	0	0
TOTAL	14	48.27	11	37.93	4	13.79	29	100.0	32	100.0

oocytes. The second subgroup consisted of women who underwent IVF with donated oocytes. The third subgroup consisted of women who received an embryo donation. The study group was divided into three age subgroups: 40-44 years, 45-49 years, and 50-54 years.

Maternal morbidity was defined by the following outcomes: pregnancy-induced hypertension (PIH), chronic hypertension, pre-gestational and gestational diabetes mellitus (GDM), spontaneous abortion, intrauterine growth restriction (IUGR), type of pregnancy (singleton or multiple), preterm birth (< 37 weeks), abruptio placentae, placenta previa, and type of delivery. Postpartum complications were defined by the following outcomes: postpartum hemorrhage, postpartum hysterectomy, postpartum blood transfusion, postpartum fever, and average hospital stay. Neonatal outcomes were defined by the following: gestational age, birth weight, five-minute Apgar score, hyperbilirubinemia, respiratory distress syndrome (RDS), meconium aspiration, intracranial hemorrhage, minor and major congenital anomalies, and admission to the neonatal intensive care unit (NICU).

The collected data was statistically analyzed and compared to the results of previous studies. The data was analyzed using descriptive and analytic statistical methods. The descriptive statistical measures included the mean, standard deviation, and minimum and maximum values. Analytic statistical methods included Student's *t*-test, Chi-squared test, Fischer's exact test, and one-way analysis of variance (ANOVA). Statistical analysis was done using the SPSS software, version 10.0.

## Results

Twenty-nine women in the study group, aged 40-54 years, conceived using IVF, either with own oocytes or donated oocytes/embryo. The control group consisted of 32 women, who spontaneously conceived during a normal menstrual cycle. The study and control groups consisted of 69.31% and 37.50% of nulliparous women, respectively.

One previous gynecologic surgery was noted in the medical history of 62.06% and 15.62% women in the study and control group, respectively. The large difference in the number

of women who had one previous gynecologic surgery was statistically significant between the study and control group [ $\chi^2=13.971$ ,  $p < 0.001$ ]; OR = 8.836 (95% CI: 2.625-29.744)]. Myomectomy, conization of the cervix, and tubal surgery were performed in 17.24%, 20.68%, and 24.14% of women in the study group, respectively. In the control group, myomectomy and conization of the cervix were performed in 6.26% of women, while 3.13% of women had a tubal surgery.

The largest proportion of the study group was in the 40-44 years age subgroup (48.27%), followed by the 45-49 years age subgroup (37.93%), and the smallest proportion of women were in the 50-54 years age subgroup (13.79%). The differences between the age subcategories are not statistically significant ( $p > 0.05$ ). Proportion of study group women compared to age category and method of conception are demonstrated in Table 1.

In the study group of 29 women, 20.66% conceived by IVF-ICSI using own oocytes, 68.96% conceived by IVF with donated oocytes, and 10.34% conceived using donated embryos. Women, who underwent IVF using donated oocytes and embryos, were older compared to women, who conceived by IVF using their own oocytes. There was a statistically significant difference between the conception method subgroups ( $\chi^2 = 28.120$ ,  $p < 0.001$ ), which implies that the largest proportion of women conceived by IVF using donated oocytes, and the smallest proportion conceived using donated embryos. Depending on the age category, there was a statistically significant difference between the conception method subgroups ( $\chi^2 = 13.878$ ,  $p < 0.01$ ). When the method of conception and age are taken into consideration, most of the conceptions occurred in women, in the 45-49 years subgroup using oocyte donation.

In the study group of 29 women, 68.97% had singleton pregnancies, 27.59% had twin pregnancies, and 3.45% had

Table 3. — *Maternal complications.*

Age category (years) Complication	Study group						Control group	
	40-44		45-49		50-54		35-39	
	N	%	N	%	N	%	N	%
PIH	3	21.42	5	45.45	2	50.00	10	34.48
GDM	3	21.42	4	36.36	2	50.00	9	31.03
IUGR	1	7.14	3	27.27	1	25.00	5	17.25
PTB	5	35.71	10	90.91	4	100.0	19	65.52
SA	1	7.14	1	9.09	0	0	2	6.90
Multiple pregnancies	4	28.56	4	36.36	1	25.00	9	31.05
Other	3	21.42	4	36.36	3	75.00	10	34.48
Σ (sum)	11	78.57	10	90.90	0	0	25	86.21
None	3	21.42	1	9.09	0	0	4	13.80
TOTAL	14	100.0	11	100.0	4	100.0	29	100.0

PIH – pregnancy-induced hypertension; GDM – gestational diabetes mellitus; IUGR – intrauterine growth restriction; PTB – preterm birth; SA – spontaneous abortion.

triplet pregnancies. In the control group of 32 women, 93.75% had singleton pregnancies and 6.25% had twin pregnancies. The type of pregnancy compared to the age category in the study and control group is demonstrated in Table 2.

Twin pregnancies occurred in 24.14%, while singleton pregnancies occurred in 13.79% of women in the 45-49 years subgroup. All of these pregnancies were achieved by IVF using donor oocytes. Twin pregnancies occurred in 3.45%, while singleton pregnancies occurred in 44.82% of women in the 40-44 years subgroup; these pregnancies were achieved by IVF using own oocytes. Triplet pregnancies occurred in 3.45%, while singleton pregnancies occurred in 10.34% of women in the 50-54 years subgroup; these pregnancies were achieved using donated embryos. Twin pregnancies occurred in 6.25%, while singleton pregnancies occurred in 93.75% of women in the control group. Twin pregnancies were more frequent in the study group amongst women who received donor oocytes compared to women who did not. The difference in type of pregnancy was statistically significant between the study and the control groups ( $\chi^2 = 6.468$ ,  $p < 0.05$ ). The control group had statistically significant greater number of singleton pregnancies compared to the study group; the study group had a statistically significant greater number of multiple (twin and triplet) pregnancies compared to the control group. The frequency of certain types of pregnancies significantly differs compared to the age category ( $\chi^2 = 17.532$ ,  $p < 0.01$ ). Singleton pregnancies were the most frequent in the 40-44 years subgroup, while twin pregnancies were most frequent in the 45-49 years subgroup.

One or more pregnancy complications were found in 25 women in the study group (86.21%) and in 15 women in the control group (46.87%). The average number of complications was 1.6 in the study group, and 1.13 in the control group. The frequency of pregnancy complication was significantly different between the study and the control groups ( $p < 0.05$ ). Maternal pregnancy complications for

the study and control group are shown in Table 3.

The most frequent maternal complications were preterm birth, PIH, multiple pregnancies, gestational diabetes, and intrauterine growth restriction. All of these complications were significantly more frequent in the study group than in the control group. There was a statistically significant difference in occurrence of maternal complications between the study and the control group [ $(\chi^2 = 10.425$ ,  $p < 0.01$ ); OR = 7.083 (95% CI: 2.002-25.056)]. There was a large statistically significant difference in occurrence of maternal complications between the study and the control group; the probability of maternal complications was seven times higher in the study group compared to the control group. The proportion of preterm birth was 65.52% in the study group and 18.75% in the control group. One 50-year-old woman, treated with a cervical cerclage, had an abruptio placentae that led to a preterm birth at 28<sup>th</sup> gestational week. Preterm birth was the most frequent maternal complication amongst women in the study group ( $\chi^2 = 44.778$ ,  $p < 0.001$ ). PIH occurred more frequently within the study group, in women older than 45 years, who underwent IVF with donor oocytes/embryos compared to women who were younger than 45 years, and who underwent IVF with own oocytes. The proportion of spontaneous abortions was similar between the study and the control groups. In the study group, one woman with a triplet pregnancy had a spontaneous abortion at 20<sup>th</sup> gestational week; the second woman had a twin pregnancy and a spontaneous abortion at 23<sup>rd</sup> gestational week. Both pregnancies were achieved by IVF using donor oocytes. One abortion was medically induced at 21<sup>st</sup> gestational week, in a 41-year-old gravida, due to multiple fetal anomalies. Other maternal complication in both groups (study and control) included: pre-gestational diabetes (13.80% and 3.13%), abruptio placentae (3.45% and 0%), placenta previa (0% and 3.13%), cervical cerclage (3.45% and 3.13%), and induced abortion (3.45% and 0%). No statistically significant difference was found in occurrence of certain maternal complications among the different age sub-

Table 4. — *Gestational age of pregnancy.*

Age category (years) Gestational age	Study group						Control group	
	40-44		45-49		50-54		35-39	
	N	%	N	%	N	%	N	%
< 33 weeks	1	7.14	4	36.36	1	25.00	6	20.70
< 35 weeks	2	14.28	4	36.36	3	75.00	9	31.05
< 37 weeks	2	14.28	2	18.18	0	0	4	13.80
Σ (sum)	5	35.07	10	90.90	4	100.0	19	65.52
≥ 37 weeks	9	64.28	1	9.09	0	0	10	34.47
TOTAL	14	100.0	11	100.0	4	100.0	29	100.0

Table 5. — *Gestational age of multiple pregnancies.*

Age category Gestational age	Study group						Control group	
	40-44		45-49		50-54		35-39	
	N	%	N	%	N	%	N	%
< 28 weeks	1	7.14	1	9.09	0	0	2	6.90
< 33 weeks	1	7.14	0	0	1	25.0	1	3.13
≤ 36 weeks	2	14.28	3	27.27	0	0	5	17.25
TOTAL	4/14	28.56	4/11	36.36	1/4	25.00	9/29	31.05

groups ( $\chi^2 = 1.531, p > 0.05$ ).

According to the gestational age of pregnancy, the study and control groups were subdivided into those that lasted less than 33 weeks, less than 35 weeks, and less than 37 weeks. Gestational age according to age subgroups is shown in Table 4.

In the study group, gestational age was less than 33 weeks in 20.70%, less than 35 weeks in 31.05%, and less than 37 weeks in 13.80%. In the control group, gestational age was less than 33 weeks in 3.13%, less than 35 weeks in 6.25%, and less than 37 weeks in 9.37%. The study group had a higher frequency of pregnancies, which lasted less than 33 and 35 weeks compared to the control group. A total of 65.52% of pregnancies in the study group, and 18.75% from the control group, had a gestational age less than 37 weeks. There was a statistically significant difference in the proportion of pregnancies with a gestational age less than 37 weeks between the study and control group [ $\chi^2 = 13.757, p < 0.001$ ]; OR = 8.233 (95% CI: 2.549-26.584)]. This implied a large statistically significant difference in proportion of pregnancies lasting less than 37 weeks between the study and the control group; the study group has an eight-times higher probability of labour and delivery before 37<sup>th</sup> week. There was no statistically significant difference in duration of pregnancy between the age groups ( $\chi^2 = 3.263, p > 0.05$ ). The proportion of pregnancies lasting less than 37 weeks did not differ between the age groups ( $p > 0.05$ ).

The study group had a greater proportion of multiple pregnancies compared to the control group. Gestational age of multiple pregnancies according to the age group is demonstrated in Table 5. Multiple pregnancies were present in 31.05% of women in the study group, and in 6.25% of women in the control group. There was a large statisti-

cally significant difference between the two groups [ $\chi^2 = 6.322, p < 0.05$ ]; OR = 6.750 (95% CI: 1.318-34.565)]. The study group had a 6.7-times higher probability of multiple pregnancies than the control group. The study group had a total of nine multiple pregnancies, eight of these were twin pregnancies, while one was a triplet pregnancy. The pregnancy was terminated by a spontaneous abortion before the 28<sup>th</sup> week in 6.90% of women in the study group. One case was triplet pregnancy in a 41-year-old woman, which ended with a spontaneous abortion in the 20<sup>th</sup> gestational week. The other case was that of a twin pregnancy in a 48-year-old woman. In the study group, 6.90% of pregnancies had a gestational age less than 33 weeks and 17.25% of pregnancies had a gestational age less than 36 weeks. In the control group, 3.13% of pregnancies had a gestational age less than 33 weeks, and the same proportion had a gestational age less than 36 weeks. No statistically significant difference was found in the proportion of multiple pregnancies and gestational age between the two groups ( $\chi^2 = 0.917, p > 0.05$ ). The reason behind this was a small proportion of pregnancies with a gestational age ≤ 36 weeks in the control group.

Twenty-six deliveries occurred in the study group, while the control group had 32 deliveries. The type of delivery and postpartum complications are demonstrated in Table 6. Cesarean section (CS) was performed in 84.62% of women in the study group, and 21.87% of women in the control group. Elective CS was performed in 76.92% and 6.25% of women in the study and control group, respectively. Emergency CS was performed in 7.69% and 15.63% of women in the study and control group, respectively. The most common indications for CS were nulliparity and an older age, multiple pregnancies and preterm birth, risk of fetal asphyxia, and hypertensive disease in pregnancy.



Table 6. — *Type of delivery and postpartum complications.*

Age category (years)	Study group						Control group	
	40-44		45-49		50-54		35-39	
	N	%	N	%	N	%	N	%
Vaginal delivery	4	33.33	0	0	0	0	4	15.38
Caesarean section	8	66.66	10	100.0	4	100.0	22	84.62
Postpartum hemorrhage	1	8.33	1	10.00	0	0	2	7.69
Postpartum hysterectomy	0	0	1	10.00	0	0	1	3.85
Blood transfusion	1	8.33	1	10.00	1	25.00	3	11.54
Postpartum fever	1	8.33	1	10.00	1	25.00	3	11.54
Average hospital stay (days)	4.3 ± 3.8		4.5 ± 3.9		5.2 ± 3.5		4.5 ± 3.6	
Total number of deliveries	12	100.0	10	100.0	4	100.0	26	100.0

Table 7. — *Neonatal outcomes.*

Age category (years)	Study group						Control group	
	40-44		45-49		50-54		35-39	
	N	%	N	%	N	%	N	%
Average GA (weeks)	37.4±1.3		36.1±0.9		33.6±0.8		35.2±0.9	
< 1,500 grams	2	14.28	3	17.63	1	25.00	6	17.16
< 2,500 grams	2	14.28	4	23.53	2	50.00	8	22.86
≥ 2,500 grams	3	21.42	3	17.63	1	25.00	7	20.00
≥ 3,500 grams	7	50.00	7	41.17	0	0	14	40.00
Apgar < 7 (5 minutes)	3	21.42	4	23.53	1	25.00	8	22.86
SGA	2	14.28	2	11.76	0	0	4	11.43
Hyperbilirubinemia	2	14.28	3	17.63	1	25.00	6	17.14
Meconium aspiration	0	0	1	5.88	0	0	1	2.86
RDS	0	0	2	11.76	1	25.00	3	8.57
ICH	1	7.14	2	11.76	1	25.00	3	8.57
Minor CA	1	7.14	1	5.88	0	0	2	5.72
Major CA	1	7.14	0	0	0	0	1	2.86
NICU admission	2	14.28	3	17.63	3	75.00	8	22.86
Total	14	100.0	17	100.0	4	100.0	35	100.0

GA – gestational age; SGA – small for gestational age; RDS – respiratory distress syndrome; ICH –intracranial hemorrhage; CA – congenital anomaly; NICU – neonatal intensive care unit.

There were 15.38% vaginal deliveries in the study group and 78.13% in the control group. There is a large statistically significant difference in the type of delivery between the study and the control groups [ $\chi^2 = 22.587$ ,  $p < 0.001$ ; OR = 19.643 (95% CI: 5.064-76.190)]. CS were significantly more common in the study group than in the control group; the study group had 19.6-times higher probability of CS than the control group.

Postpartum hemorrhage occurred in 7.69% of women and 3.13% of women in the study and control group, respectively. Due to a high degree of postpartum blood loss, a hysterectomy was indicated in one woman. Postpartum blood transfusion was received by 11.54% of women and 6.25% of women in the study and control group, respectively. The length of average hospital stay was similar between the age subgroups in the study group. The length of stay was shorter for women in the control group than for women in the study group. No statistically significant difference was found in the average length of hospital stay between the study and the control groups ( $t = 0.831$ ,  $p >$

0.05). The lack of statistical significance was almost certainly due to large standard deviation in the length of hospital stay.

Thirty-five live births resulted from the 26 deliveries in the study group. Thirty-six live births resulted from 32 deliveries in the control group. Neonatal outcomes are demonstrated in Table 7. The average gestational age for newborns in the study group was  $35.2 \pm 0.9$  weeks, while the average was  $38.3 \pm 1.1$  weeks for the newborns in the control group. The difference in gestational age of newborns was statistically significant between the study and the control group ( $t = 13.013$ ,  $p < 0.001$ ). The average gestational age was the shortest in the 50-54 years subgroup of the study group, while it was the longest in the 40-44 years subgroup. The difference in gestational age was statistically significant between the age subgroups ( $p < 0.01$ ). Age subgroup comparisons are as follows: 40-44 vs. 45-49 ( $t = 3.168$ ,  $p < 0.01$ ); 40-44 vs. 50-54 ( $t = 7.172$ ,  $p < 0.001$ ); 45-49 vs. 50-54 ( $t = 5.486$ ,  $p < 0.01$ ). Very low birth weight (VLBW < 1,500 grams) and low birth weight (LBW < 2,500 grams)

was present in 17.16% and 22.86% newborns of the study group, respectively. Very low birth weight (< 1,500 grams) and low birth weight (< 2,500 grams) was present in 5.55% and 8.33% newborns of the control group, respectively. All very low birth weight newborns were from pregnancies with a gestational age less than 33 weeks. The difference in birth weight was statistically significant between the study and the control group [ $\chi^2=7.360$ ,  $p < 0.01$ ]; OR = 4.650 (95% CI: 1.461-14.800)]. The statistically significant difference is large in low birth weight (< 2500 grams) between the study and the control group; the study group had a 4.65-times higher probability of a low birth weight newborn. The five-minute Apgar score was < 7 in 22.86% and 19.44% of newborns in the study and control group, respectively; the difference was not statistically significant between the groups ( $p > 0.05$ ). The frequency of hyperbilirubinemia, meconium aspiration, respiratory distress syndrome, intracranial hemorrhage, and minor and major congenital anomalies was similar between the study and control group.

## Discussion

Due to development and advancement of certain ART procedures in the past 30 years, there is a greater proportion of older women who are becoming pregnant. The present prospective study examined the maternal complications, complications of labour and delivery, and neonatal outcomes in 29 women, aged 40-54 years, who had conceived by IVF, either using own oocytes or donated oocytes/embryos. The control group consisted of 32 women, aged 35-39 years, who achieved a spontaneous pregnancy during a normal menstrual cycle. The largest proportion of women in the study group were in the 40-44 years subgroup (48.27%), followed by those women in the 45-49 years subgroup (37.93%), and a smallest proportion of women in the 50-54 years subgroup (13.79%). The study group was composed of 69.13% nulliparous women, while the control group had 40.25% nulliparous women. Other authors have found a proportion of 33.10% of nulliparity amongst women aged 40-44 years, while this proportion was 39.00% in women aged more than 45 years [6]. As age increases, especially over the age of 45 years, the present study showed an increase in maternal complications, such as PIH, chronic hypertension, pre-gestational and gestational diabetes mellitus, IUGR, and preterm birth (PTB). The frequency of certain maternal complications, in the study and control group, is as follows: PIH (34.48%, 6.25%), chronic hypertension (10.35%, 3.13%), pre-GDM (13.80%, 3.13%), GDM (31.03%, 6.25%), IUGR (17.25%, 6.25%), and preterm birth (65.52%, 18.75%). All of the aforementioned maternal complications were significantly more frequent in the study than in the control group ( $p < 0.01$ ). Other authors have found the frequency of maternal complications, in women older than 43 years, who underwent IVF, to be 8.7% for PIH (preeclampsia), 6.1% for GDM, 20.2% for PTB, and 8.2%

for very preterm birth (< 33 gestational weeks) [9]. In women, aged 40-44 years, the frequency of maternal complications was 2.4% for preeclampsia, 2.7% for chronic hypertension, 1.4% for pre-gestational diabetes, and 10.2% for gestational diabetes. In women, over the age of 45 years, the frequency of maternal complications was 10.7% for preeclampsia, 6.8% for chronic hypertension, 4.5% for pre-GDM, and 17.0% for GDM. In both age group, all methods of conception were encompassed [6]. The frequency of maternal complications was examined by a study, which encompassed women who underwent IVF using donor oocytes. The age distribution of these women was such that 50% of women were older than 43 years and 30.6% of women were older than 45 years. PIH was found in 27.6% of women, GDM in 23.9% of women, CS was performed in 72.0% of women, PTB occurred in 14.9% of women, 7.6% of newborns were small for gestational age, while 2.2% of newborns had major malformations [10]. Another study found the frequency of preeclampsia to be 16.0% in women, who conceived using donor oocytes, which increased to 25.00% in women, who conceived using donated embryos, while the frequency was 3.7% in the control group [11]. Development of preeclampsia is postulated to be due to an immunologic maladaptation of the pregnant woman.

The frequency of multiple pregnancies was 31.03% and 6.25% in the study and control group, respectively. The difference in frequency of multiple pregnancies was statistically significant between the two groups ( $p < 0.01$ ). In the study group, all multiple pregnancies occurred in women who received an oocyte donation. All twin pregnancies in the study and the control groups ended with a delivery before 36<sup>th</sup> gestational week. Some authors have found that after IVF, the frequency of twin and triplet pregnancies was 21.0% and 0.8%, respectively [12]. Women, who achieved a pregnancy by IVF using donated oocytes, are at an increased risk of multiple pregnancies and preterm birth [13]. The frequency of twin pregnancies in women, who achieved pregnancy by IVF using donor oocytes, is 39.4% compared to 15.0% in women, who conceived using IVF without donor oocytes [9]. The proportion of multiple pregnancies in women, older than 41 years, who underwent IVF, is 6.6% [14]. In order to decrease the proportion of multiple pregnancies after IVF-ET (embryo transfer), many authors recommend an elective transfer of one, good quality embryo. Transfer of more than one embryo increases the pregnancy rate, but it also increases the rate of multiple pregnancies. In women, aged 40, 41, 42, and 43 years, who underwent IVF with one embryo transfer, the rate of pregnancy was 11%, 8%, 5%, 11%, respectively. The rate of pregnancy was 21%, 16%, 9%, and 9% for women of the same age, respectively, but in this case they received two ETs. The rate of multiple pregnancies for these women was 20%, 14%, 28%, and 0%, respectively [15]. Twin pregnancies are associated with an increased risk of preterm birth in women who underwent

IVF, with or without donor oocytes.

The proportion of spontaneous abortions was 6.90% and 6.25% in the study and control group, respectively. The frequency of spontaneous abortions was 7.14% in the 40–44 years subgroup and 9.09% in the 45–49 years subgroup. The frequency of spontaneous abortion in 40-year-old women, who underwent IVF was 32.6% [2]. The frequency of spontaneous abortion in women, who conceived by IVF with donor oocytes, was 16.9% in the 40–44 years subgroup, 18.5% in 45–49 years subgroup, and 19% in the  $\geq 50$  years subgroup [16].

The frequency of preterm birth was 65.5% in the present study group composed of early preterm birth ( $< 33$  weeks) in 20.70% of cases, moderate preterm birth ( $< 35$  weeks) in 31.05% cases, and late preterm birth ( $< 37$  weeks) in 13.80% of cases. The frequency of early preterm birth, moderate preterm birth, and very late preterm birth was 3.13%, 6.25%, and 9.37% in the control group, respectively. The difference in frequency of preterm birth was statistically significant between the study and control group ( $p < 0.01$ ). Prematurity significantly increases the proportion of neonatal complications. The following rates of preterm birth were reported in pregnancies achieved by various ART procedures: 7.2% of singleton and 46.7% of twin pregnancies ( $< 37$  weeks); 1.2% of singleton and 7.5% of twin pregnancies ( $< 32$  weeks) [7].

The frequency of very low birth weight ( $< 1,500$  grams) and low birth weight ( $< 2,500$  grams) was 17.16% and 22.86% in the present study group, respectively. The frequency of very low birth weight ( $< 1,500$  grams) and low birth weight ( $< 2,500$  grams) was 5.55% and 8.33% in the present control group, respectively. Other authors have found the birth weight to be  $< 1,000$  grams in 2.6% newborns and  $< 2,500$  grams in 25.8% newborns, in a population of women who underwent IVF [9]. Newborns, from singleton, IVF pregnancies, had a frequency of VLBW and LBW of 1.3% and 4.6%, respectively. Newborns, from twin, IVF pregnancies, had a frequency of VLBW and LBW of 5.3% and 38.8%, respectively [7]. Low birth weight was significantly more frequent in twin than in singleton newborns, from IVF pregnancies, because the rate of preterm birth was significantly higher in twin pregnancies. The present study found a five-minute Apgar score  $< 7$  in 22.86% and 13.88% of newborns in the study and control group, respectively; the difference was not statistically significant between the two groups ( $p > 0.05$ ). Meconium aspiration occurred in 2.86% of newborns from the study group, while RDS occurred in 8.57% and 2.77% of newborns born to the study and control group, respectively. NICU admissions included 22.86% and 8.33% of newborns from the study and control group, respectively. Other authors report the rate of neonatal complications in newborns from singleton, IVF pregnancies to be 1.6% for an Apgar  $< 7$ , 4.5% for RDS, 0.2% for meconium aspiration, and the rate, for the same neonatal complications in new-

borns from twin pregnancies was 3.0%, 16.2%, and 0.1%, respectively [7].

High proportions of preterm birth, multiple pregnancies, PIH, nulliparity, and older age contributed to a high proportion of CS (84.62%) in the present study group; this proportion was 21.87% in the control group. There was a large, statistically significant difference in proportion of CS between the study and the control group ( $p < 0.01$ ). The proportion of CS in women after IVF was found to be 42.9% in those aged 40–44 years, and 78.5% in those older than 45 years [6]. The proportion of CS in older women, after IVF with donor oocytes, was found to be 61% [9] and 70.8% [17]. The frequency of antepartum hemorrhage due to abruptio placentae was 3.45% in the study group. Placenta previa was diagnosed in 3.13% of women in the control group. The frequency of abruptio placentae and placenta previa in singleton pregnancies after IVF was 1.3% and 2.9%, respectively, while the frequency of the same maternal complications in twin pregnancies after IVF was 1.4% and 0.9%, respectively [7].

Postpartum complications included postpartum hemorrhage, postpartum blood transfusions, and postpartum fever. The frequency of postpartum blood transfusion was 11.54% and 6.25% of women in the present study and control group, respectively. Other studies have found that postpartum blood transfusion was required by 1.1% of women, older than 45 years, who conceived by IVF [17]. Postpartum hemorrhage occurred in 7.69% and 3.13% of women in the study and control group, respectively. Other authors have found the frequency of postpartum hemorrhage in older gravidas, who underwent ART to be 4% [6], 5.9% [17], and 7.4% [9]. A postpartum hysterectomy was performed in one woman from the study group due to heavy bleeding and uterine atony. Other authors performed postpartum hysterectomy in 0.5% of women, older than 47 years, who underwent IVF [17].

## Conclusion

Pregnancies in 40-year-old or older women, achieved by IVF, were associated with a higher risk for development of maternal complications in pregnancy, and during delivery, as well as a higher risk for development of neonatal complications, compared to pregnancies achieved spontaneously in 35- to 39-year-old women. Multiple pregnancies significantly increase the proportion of maternal and neonatal complications.

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