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ASSISTED REPRODUCTION TECHNOLOGIES

Obstetric and perinatal complications associated with assisted reproductive treatment in Spain

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Abstract

Background Although most newborns conceived through assisted reproductive treatments are healthy, there are concerns about the safety of reproductive techniques and their effect on foetal/maternal well-being.

Objective This study aims to describe the incidence of obstetric and perinatal complications in women undergoing assisted reproductive treatments in the Spanish Health System.

Method This is a cross-sectional observational study aimed at women who have been mothers between 2013 and 2018 in Spain. The data was collected through an online survey of 42 items that was distributed through lactation associations and postpartum support groups. In the data analysis, crude odds ratios (OR) and adjusted odds ratios (AOR) were calculated, through a multivariate analysis with binary logistic regression and multinomial logistic regression.

Results Five thousand nine hundred forty-two women participated, 2.3% (139) through artificial insemination and 8.2% (486) through in vitro fertilisation (IVF) techniques. Women who underwent IVF had a higher likelihood of suffering problems during pregnancy (OR = 1.71; 95% confidence intervals (95% CI), 1.37–2.13), delivery (OR = 1.43; 95% CI, 1.01–2.02), and postpartum (OR = 1.94; 95% CI, 1.40–2.69) than women with spontaneous pregnancy. No increased likelihood of neonatal problems was observed in this group except for twin pregnancy (OR = 9.17; 95% CI, 6.02–13.96) and prematurity (OR = 1.43; 95% CI, 1.01–2.02). No differences were observed between spontaneous pregnancies and those achieved by artificial insemination.

Conclusions Pregnancies achieved through IVF present a higher risk of complications before, during and after delivery. However, there is no increased risk of neonatal problems except for a higher likelihood of twin pregnancy and prematurity.

Keywords Reproductive techniques assisted · Fertilization in vitro · Quality of health care · Patient safety · Obstetric labour complications · Morbidity

Introduction

Infertility affects approximately 10–15% of the world's reproductive age population [1], with a prevalence of between 10 and 12% at European level [2]. The latest estimates indicate that more than 1.6 million of assisted reproduction cycles worldwide are carried out each year, and more than 5 million children have already been born using these techniques [3]. As

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a result of the advances in these techniques and a better accessibility to these services, the number of children born through assisted reproductive techniques (ART) has continued to increase [4], resulting in an increase in the number of multiple pregnancies and births [5].

In 1978, the first baby conceived through artificial insemination, Louise Joy Brown, was born in England. Gestation was considered of high risk because the mother developed pre-eclampsia and the responsible gynaecologist did not want to risk a normal delivery and decided to perform a C-section at week 38 [5]. This example highlights the fact that gestations through assisted reproductive techniques are associated with increased perinatal risk [5, 6].

Most newborns conceived through ART are healthy, but these have also been associated with higher rates of adverse obstetric and perinatal outcomes [7–9]. Concern about the safety of reproductive techniques and their effect on foetal/maternal well-being is growing [10]. It is well documented that pregnancies achieved through ART represent a significant increase in the risk of multiple pregnancies and adverse perinatal outcomes. Some studies suggest an increased risk of pre-eclampsia, gestational hypertension, placenta praevia and diabetes [6, 11–13]. An increase in the incidence of impaired foetal growth, premature births and frequency of intrauterine death has been observed regarding perinatal outcomes as compared with the average of all pregnancies [5, 14]. In addition, post-IVF pregnancies have significantly higher rates of induced births and C-sections [5].

The main factors associated with these adverse outcomes were multiple pregnancies and births [15]. However, as unique embryo transfers become widespread, these figures decrease, but unique gestations still have a higher incidence of adverse outcomes as compared with spontaneous pregnancies [16].

Different studies conducted at European and North American levels show the current interest in the use of these techniques and their success rates [17, 18]. However, studies focusing on neonatal maternal outcomes of pregnant women by assisted reproductive techniques are scarcer, and although the literature relates ART and maternal and neonatal outcomes, not all of the studies consider factors such as maternal age and other relevant variables such as obstetric clinical records [11], and the underlying cause of these results is still being discussed. It is still not clear whether poorest perinatal outcomes are mainly due to the characteristics of the parents or whether assisted reproductive techniques are a contributing factor in themselves [19].

It is undeniable that ART is increasingly present in society, and this makes it important to know the obstetric and perinatal risks involved in order to be able to provide the best assistance. For these reasons, in this study, we have considered describing the incidence of obstetric and perinatal complications in women undergoing assisted reproductive treatments in the Spanish Health as compared with women with a spontaneous pregnancy.

Material and method

Design and selection of the study subjects

This is a cross-sectional observational study aimed at women who have been mothers between 2013 and 2018 in Spain. The survey completion was made between January 2019 and June 2019. This study has received the approval of the Ethics and Clinical Research Committee of Alcázar de San Juan, in Spain, with protocol number 92-C.

The participants were women over the age of 18, who understood Spanish and who agreed to fill in the questionnaire. Before filling in the questionnaire, the participants had to read the information sheet about the purpose of the study and give their consent to participate in it. Survey recipients were informed that the overall objective of the study was to determine the relationship between complications that occur after childbirth, the prevalence of breastfeeding and the factors that may be associated with these phenomena so that their answers were not conditioned by the fact that they had received a fertility treatment. After this, they were provided with the necessary information to be able to complete the questionnaire, including a brief explanation in less-technical language of each of the items surveyed. Participants were told that that the questions related to the last pregnancy and the weight reported was expected to be before pregnancy. Participants could voluntarily provide an e-mail address or phone number through which they would be contacted in case any additional information related to the study was needed.

For the sample size estimation, the maximum modelling criterion that requires ten events for each independent variable to be included in the multivariate model has been used [20]. We have considered, as a reference event for the sample estimate, twin pregnancy, which amounts to around 3% of the general population [21]. Considering a minimum of ten independent variables, a minimum of 100 women with twin pregnancies would be required, representing a minimum total population of 3333 women under study within this scenario.

For data collection, an anonymous online questionnaire was designed with 42 items (30 yes/no questions and 12 multiple answer questions) on sociodemographic variables, obstetric variables, and complications during pregnancy, delivery and postpartum. The time needed to fill in the questionnaire was 12–15 min. The answer options for the pathologies were Yes and No. In the instructions, the participants were informed of the possibility of stating No in those questions that raised some doubts. The objective of this procedure was to avoid overstating the pathologies on the one hand, and to

Table 1 Sociodemographic and obstetric characteristics of the women according to the type of pregnancy

Variable	Type of conception			
	Spontaneous (*n* (%))	Insemination (*n* (%))	IVF	*P* value[a]
Maternal age				
< 25 years	152 (2.9)	0 (0.0)	0 (0.0)	< 0.001
25–35 years	3263 (61.4)	66 (47.5)	139 (28.6)	
> 35 years	1902 (35.8)	172 (52.5)	253 (71.4)	
Level of education				
None	7 (0.1)	0 (0.0)	1 (0.2)	< 0.001
Primary	95 (1.8)	1 (0.7)	12 (2.5)	
Secondary	1491 (28.0)	47 (33.8)	86 (17.7)	
University	3724 (70.0)	91 (65.5)	387 (70.6)	
Monthly family income (euros)				
< 1000	310 (5.8)	11 (7.9)	17 (3.5)	0.003
1000–2000	1794 (33.7)	51 (36.7)	129 (33.2)	
2000–3000	1801 (33.9)	47 (33.8)	180 (37.0)	
3000–4000	992 (18.7)	23 (16.5)	109 (22.4)	
> 4000	420 (7.9)	7 (5.0)	51 (10.5)	
Nationality				
Spanish	4978 (93.6)	134 (96.4)	460 (93.8)	0.288
Foreign	339 (6.4)	5 (3.6)	26 (5.3)	
BMI				
Normal	1454 (27.6)	36 (26.1)	131 (27.2)	0.919
Overweight	2428 (46.1)	63 (45.7)	230 (47.8)	
Obese	1383 (26.3)	39 (28.3)	120 (24.9)	
Attendance to ME				
No	1264 (23.8)	15 (10.8)	80 (16.5)	< 0.001
Yes	4053 (76.2)	124 (89.2)	406 (83.5)	
Pre-pregnancy smoking habits				
No	4029 (76.2)	101 (72.7)	407 (83.7)	< 0.001
Yes	1268 (23.8)	38 (27.3)	79 (16.3)	
Number of pregnancies				
1	2727 (51.3)	116 (83.5)	318 (65.4)	< 0.001
2	1860 (35.0)	19 (13.7)	104 (21.4)	
3	496 (9.3)	4 (2.9)	40 (8.2)	
4	154 (2.9)	0 (0.0)	17 (3.5)	
5 or more	80 (1.5)	0 (0.0)	7 (1.4)	
Number of deliveries				
None	1097 (20.6)	38 (27.3)	174 (35.8)	< 0.001
1	2651 (49.9)	96 (69.1)	261 (53.7)	
2	1370 (25.8)	5 (3.6)	46 (9.5)	
3	170 (3.2)	0 (0.0)	5 (1.0)	
4	24 (0.5)	0 (0.0)	0 (0.0)	
5 or more	5 (0.1)	0 (0.0)	0 (0.0)	

[a] Pearson's χ^2 test

minimise the number of subjects excluded for the subsequent multivariate analysis on the other hand. The questionnaire was disseminated among the Spanish lactation and postpartum support associations and groups, and those responsible for these groups were in charge of disseminating them among their members. From that moment on, a snowball recruitment phase began, as the participants themselves could send the form to other mothers. The online questionnaire was made available to mothers between January and June 2019.

The variables included in the study were:

The primary dependent variable was the type of conception (spontaneous, artificial insemination or in vitro fertilisation).

Table 2 Complications during pregnancy according to the type of pregnancy

Variable	Type of conception		
	Spontaneous (*n* (%))	Insemination (*n* (%))	IVF
Twin pregnancy			
No	4977 (93.6)	128 (92.1)	425 (87.4)
Yes	340 (6.4)	11 (7.9)	61 (12.6)
OR (95% CI)	1 (ref.)	*5.01 (2.54–9.89)*	*8.08 (5.65–11.56)*
AOR[a] (95% CI)	1 (ref.)	*5.95 (2.93–12.09)*	*9.17 (6.02–13.96)*
Prematurity			
> 37	4977 (93.6)	128 (92.1)	425 (87.5)
< 37	81 (1.5)	10 (7.2)	54 (11.1)
OR (95% CI)	1 (ref.)	1.26 (0.67–2.35)	*2.10 (1.57–2.81)*
AOR[b] (95% CI)	1 (ref.)	1.05 (0.54–2.04)	*1.43 (1.01–2.02)*
Hypertensive states			
No	4981 (93.7)	133 (95.7)	420 (86.4)
Yes	336 (6.3)	6 (4.3)	66 (13.6)
OR (95% CI)	1 (ref.)	0.67 (0.29–1.53)	*2.33 (1.76–3.09)*
AOR[c] (95% CI)	1 (ref.)	0.49 (0.21–1.13)	*1.98 (1.44–2.73)*
Gestational diabetes—diet			
No	4714 (88.7)	125 (89.9)	397 (81.7)
Yes	603 (11.3)	14 (10.1)	89 (18.3)
OR (95% CI)	1 (ref.)	0.88 (0.50–1.53)	*1.75 (1.37–2.24)*
AOR[c] (95% CI)	1 (ref.)	0.73 (0.41–1.30)	*1.45 (1.11–1.90)*
Gestational diabetes—insulin			
No	5194 (97.7)	135 (97.1)	463 (95.3)
Yes	123 (2.3)	4 (2.9)	23 (4.7)
OR (95% CI)	1 (ref.)	1.25 (0.46–3.44)	*2.10 (1.33–3.31)*
AOR (95% CI)	1 (ref.)	1.07 (0.38–2.30)	1.64 (0.98–2.74)
Hyperthyroidism			
No	5068 (95.3)	129 (92.8)	460 (94.7)
Yes	249 (4.7)	10 (7.2)	26 (5.3)
OR (95% CI)	1 (ref.)	1.58 (0.82–3.04)	1.15 (0.76–1.74)
AOR[c] (95% CI)	1 (ref.)	1.38 (0.70–2.68)	1.16 (0.74–1.81)
Hypothyroidism			
No	4657 (87.6)	113 (81.3)	385 (79.2)
Yes	660 (12.4)	26 (18.7)	101 (20.8)
OR (95% CI)	1 (ref.)	1.62 (1.05–2.51)	*1.85 (1.47–2.34)*
AOR[c] (95% CI)	1 (ref.)	1.53 (0.98–2.38)	*1.64 (1.27–2.11)*
Anaemia			
No	3224 (60.6)	85 (61.2)	288 (59.3)
Yes	2093 (39.4)	54 (38.8)	198 (40.7)
OR (95% CI)	1 (ref.)	0.98 (0.69–1.38)	1.06 (0.88–1.28)
AOR[c] (95% CI)	1 (ref.)	1.04 (0.73–1.48)	1.11 (0.91–1.36)
Intrahepatic cholestasis			
No	5254 (98.8)	136 (97.8)	479 (98.6)
Yes	63 (1.2)	3 (2.2)	7 (1.4)
OR (95% CI)	1 (ref.)	1.84 (0.57–5.93)	1.22 (0.56–2.68)
AOR[c] (95% CI)	1 (ref.)	2.09 (0.62–6.99)	1.19 (0.50–2.81)
Risk of preterm birth			
No	4892 (92.0)	129 (92.8)	431 (88.7)

Table 2 (continued)

Variable	Type of conception		
	Spontaneous (*n* (%))	Insemination (*n* (%))	IVF
Yes	425 (8.0)	10 (7.2)	55 (11.3)
OR (95% CI)	1 (ref.)	0.89 (0.47–1.71)	*1.47 (1.09–1.98)*
AOR[c] (95% CI)	1 (ref.)	1.08 (0.55–2.10)	*1.58 (1.28–2.22)*
Deep vein thrombosis			
No	5247 (98.7)	139 (100.0)	479 (98.6)
Yes	70 (1.3)	0 (0.0)	7 (1.4)
OR (95% CI)	1 (ref.)	NC	1.10 (0.50–2.40)
AOR[c] (95% CI)	1 (ref.)	NC	1.10 (0.48–2.54)
Oligoamines			
No	5116 (96.2)	133 (95.7)	467 (96.1)
Yes	201 (3.8)	6 (4.3)	19 (3.9)
OR (95% CI)	1 (ref.)	1.15 (0.50–2.63)	1.04 (0.64–1.67)
AOR[c] (95% CI)	1 (ref.)	1.05 (0.45–2.45)	0.98 (0.59–1.65)
Polyhydramnios			
No	4858 (91.4)	125 (89.9)	443 (91.2)
Yes	459 (8.6)	14 (10.1)	43 (8.8)
OR (95% CI)	1 (ref.)	1.19 (0.68–2.08)	1.03 (0.74–1.43)
AOR[c] (95% CI)	1 (ref.)	1.21 (0.68–2.14)	1.14 (0.80–1.62)
Composite pregnancy morbidity			
No	2055 (38.6)	56 (40.3)	129 (26.5)
Yes	3262 (61.4)	83 (59.3)	357 (73.5)
OR (95% CI)	1 (ref.)	0.93 (0.66–1.32)	*1.74 (1.42–2.15)*
AOR[c] (95% CI)	1 (ref.)	0.93 (0.66–1.33)	*1.71 (1.37–2.13)*

[a] Adjusted by maternal age, BMI and nulliparity

[b] Adjusted by maternal age, BMI, and nulliparity + twin pregnancy, smoking habit, economic income, level of education, nationality and pregnancy complications

[c] Adjusted by maternal age, BMI, and nulliparity + twin pregnancy, smoking habit, economic income, level of education, nationality and maternity training

Italic font indicates statistically significant differences

The independent adjustment variables were maternal age, income level, level of education, tobacco consumption, body mass index (BMI), number of children, number of births, gestational age at the time of delivery, pre-eclampsia during pregnancy, diet-controlled gestational diabetes, insulin-controlled gestational diabetes, hyperthyroidism, hypothyroidism, anaemia, intrahepatic cholestasis, risk of preterm birth, deep vein thrombosis, oligoamines, polyhydramnios, altered foetal heart rate (FHR) during delivery, stained amniotic fluid (AF), vaginal bleeding, non-progression of delivery, cephalopelvic disproportion, intrapartum fever, intrapartum pre-eclampsia, induced delivery, end of delivery, episiotomy, tearing, skin-to-skin contact, breastfeeding (BF), low weight (2.500 g), macrosomia (> 4.000 g), newborn admission (RN), type of feeding at discharge, postpartum-related subsequent maternal surgery, maternal admission into intensive care unit and maternal re-admission.

In addition, four 'composite' morbidity variables were created: pregnancy (including pre-eclampsia during pregnancy, diet-controlled gestational diabetes, insulin-controlled gestational diabetes, hyperthyroidism, hypothyroidism, anaemia, intrahepatic cholestasis, risk of preterm birth, deep vein thrombosis); delivery (including altered foetal heart rate (FHR) during delivery, stained amniotic fluid (AF), vaginal bleeding, non-progression of delivery, cephalopelvic disproportion, intrapartum fever, intrapartum pre-eclampsia, induced delivery, end of delivery by caesarean and severe tearing (types III–IV); neonatal (including prematurity, low weight (< 2.500 g), macrosomia (> 4.000 g) and maternal admission to intensive care unit; and postpartum (including

Table 3 Complications during delivery according to the type of pregnancy

Variable	Type of conception		
	Spontaneous (*n* (%))	Insemination (*n* (%))	IVF
Altered FHR			
No	4663 (87.7)	123 (88.5)	424 (87.2)
Yes	654 (12.3)	16 (11.5)	62 (12.8)
OR (95% CI)	1 (ref.)	0.93 (0.55-1.57)	1.04 (0.79–1.39)
AOR[a] (95% CI)	1 (ref.)	0.80 (0.47–1.37)	0.95 (0.70–1.28)
Stained AF			
No	4997 (94.0)	132 (95.0)	447 (92.0)
Yes	320 (6.0)	7 (5.0)	39 (8.0)
OR (95% CI)	1 (ref.)	0.83 (0.38–1.79)	1.36 (0.96–1.93)
AOR[a] (95% CI)	1 (ref.)	0.80 (0.36–1.70)	*1.50 (1.03–2.18)*
Vaginal bleeding			
No	5063 (95.2)	135 (97.1)	433 (89.1)
Yes	254 (4.8)	4 (2.9)	53 (10.9)
OR (95% CI)	1 (ref.)	0.59 (0.22–1.61)	*2.44 (1.79–3.33)*
AOR[b] (95% CI)	1 (ref.)	0.54 (0.20–1.50)	*2.10 (1.46–3.03)*
Uterine rupture			
No	5283 (99.4)	137 (98.6)	485 (99.8)
Yes	34 (0.6)	2 (1.4)	1 (0.2)
OR (95% CI)	1 (ref.)	2.27 (0.54–9.54)	0.32 (0.4–2.35)
AOR[b] (95% CI)	1 (ref.)	2.14 (0.47–9.81)	0.24 (0.03–1.96)
Non-progression of delivery			
No	4331 (81.5)	111 (79.9)	359 (73.9)
Yes	986 (18.5)	28 (20.1)	127 (26.1)
OR (95% CI)	1 (ref.)	1.11 (0.73–1.69)	*1.55 (1.26–1.94)*
AOR[a] (95% CI)	1 (ref.)	0.87 (0.60–1.36)	1.24 (0.97–1.59)
Cephalopelvic disproportion			
No	4506 (84.7)	118 (84.9)	404 (83.1)
Yes	811 (15.3)	21 (15.1)	82 (16.9)
OR (95% CI)	1 (ref.)	0.99 (0.62–1.58)	1.13 (0.88–1.45)
AOR[a] (95% CI)	1 (ref.)	0.84 (0.52–1.36)	1.09 (0.83–1.44)
Fever			
No	5040 (94.8)	131 (94.2)	450 (92.6)
Yes	277 (5.2)	8 (5.8)	36 (7.4)
OR (95% CI)	1 (ref.)	1.11 (0.54–2.29)	*1.46 (1.02–2.09)*
AOR[b] (95% CI)	1 (ref.)	0.84 (0.40–1.77)	1.46 (0.98–2.19)
Pre-eclampsia			
No	5163 (97.1)	136 (97.8)	453 (93.2)
Yes	154 (2.9)	3 (2.2)	33 (6.8)
OR (95% CI)	1 (ref.)	0.74 (0.23–2.34)	*2.44 (1.66–3.60)*
[a]AOR (95% CI)	1 (ref.)	0.52 (0.16–1.73)	*1.68 (1.03–2.73)*
Induced delivery			
No	3448 (64.8)	80 (57.6)	236 (48.6)
Yes	1869 (35.2)	59 (42.4)	250 (51.4)
OR (95% CI)	1 (ref.)	1.36 (0.97–1.91)	*1.95 (1.63–2.36)*
AOR[a] (95% CI)	1 (ref.)	1.06 (0.75–1.52)	*1.46 (1.19–1.80)*
Mode of delivery			
Eutocic	3290 (61.9)	73 (52.5)	204 (42.0)

Table 3 (continued)

Variable	Type of conception		
	Spontaneous (*n* (%))	Insemination (*n* (%))	IVF
Instrumental	837 (15.7)	28 (20.1)	99 (20.4)
OR (95% CI)	1 (ref.)	1.51 (0.96–2.35)	*1.91 (1.48–2.45)*
AOR[c] (95% CI)	1 (ref.)	0.91 (0.58–1.43)	1.24 (0.94–1.64)
Planned caesarean	388 (7.3)	10 (7.2)	70 (14.4)
OR (95% CI)	1 (ref.)	1.16 (0.60–2.27)	*2.91 (2.18–3.89)*
AOR (95% CI)	1 (ref.)	0.68 (0.33–1.40)	1.39 (0.98–1.98)
Emergency caesarean	802 (15.1)	28 (20.1)	113 (23.3)
OR (95% CI)	1 (ref.)	*1.57 (1.01–2.45)*	*2.27 (1.78–2.90)*
AOR (95% CI)	1 (ref.)	0.93 (0.58–1.50)	*1.35 (1.02–1.78)*
Episiotomy			
No	3598 (67.7)	89 (64.0)	315 (64.8)
Yes	1719 (32.3)	50 (36.0)	171 (35.2)
OR (95% CI)	1 (ref.)	1.18 (0.83–1.67)	1.14 (0.94–1.38)
AOR[d] (95% CI)	1 (ref.)	0.93 (0.63–1.35)	1.03 (0.82–1.29)
III–IV tearing			
No	5255 (988)	137 (98.6)	472 (97.1)
Yes	62 (1.2)	2 (1.4)	14 (2.9)
OR (95% CI)	1 (ref.)	1.24 (0.30–5.11)	*2.51 (1.40–4.52)*
AOR[e] (95% CI)	1 (ref.)	1.19 (0.28–5.06)	*3.19 (1.66–6.14)*
Composite morbidity delivery			
No	2008 (37.8)	42 (30.2)	109 (22.4)
Yes	3309 (62.2)	97 (69.8)	377 (77.6)
OR (95% CI)	1 (ref.)	1.40 (0.97–2.02)	*2.10 (1.68–2.62)*
AOR[f] (95% CI)	1 (ref.)	0.98 (0.67–1.45)	*1.48 (1.17–1.88)*

All the results were adjusted by the following variables: maternal age, BMI, nulliparity, twin pregnancy, maternity training, previous caesarean, newborn weight, economic income, level of education and nationality

[a] Complementary adjusted by composite pregnancy morbidity and gestational age

[b] Complementary adjusted by induced delivery, episiotomy, severe tearing and type of delivery

[c] Complementary adjusted by induced delivery

[d] Complementary adjusted by induced delivery, severe tearing and type of delivery

[e] Complementary adjusted by episiotomy and type of delivery

[f] Complementary adjusted by composite pregnancy morbidity

Italic font indicates statistically significant differencesItalic font indicates statistically significant differences

maternal postpartum surgery related to the delivery, maternal admission to intensive care unit and maternal re-admission).

Statistical analysis

First, a descriptive analysis was performed using absolute and relative frequencies for categorical variables. A bivariate analysis was then performed between the main sociodemographic and clinical characteristics regarding the type of conception, using the Pearson's chi-squared test. Then, the crude odds ratios (OR) and adjusted odds ratios (AOR) were calculated with their respective 95% confidence intervals (95% CI) to determine the relationship between the type of conception and the main problems during pregnancy, delivery and postpartum, as well as their relationship to neonatal variables. To do this, a multivariate analysis was performed by means of binary logistic regression and multinomial logistic regression (for the birth type variable). All analyses were performed using the SPSS v24.0 statistical package.

Results

The final population of study was 5942 women. Of these, 89.5% achieved a spontaneous pregnancy (5317), 2.3% (139) underwent artificial insemination to get pregnant and 8.2% (486) underwent in vitro fertilisation techniques.

Table 4 Postpartum maternal/foetal complications

Variable	Type of conception		
	Spontaneous (*n* (%))	Insemination (*n* (%))	IVF
Low weight			
No	5001 (94.2)	122 (88.4)	429 (88.6)
Yes	307 (5.8)	16 (11.6)	55 (11.4)
OR (95% CI)	1 (ref.)	*2.14 (1.25–3.64)*	*2.09 (1.54–2.83)*
AOR[a] (95% CI)	1 (ref.)	1.56 (0.86–2.84)	1.08 (0.73–1.60)
Macrosomia			
No	5067 (95.5)	133 (96.4)	458 (94.6)
Yes	241 (4.5)	5 (3.6)	26 (5.4)
OR (95% CI)	1 (ref.)	0.79 (0.32–1.95)	1.19 (0.79–1.81)
OR[a] (95% CI)		1.05 (0.42–2.64)	1.56 (0.99–2.45)
Skin-to-skin contact			
No	1122 (21.1)	31 (22.3)	161 (33.1)
Yes	541 (10.2)	21 (15.1)	66 (13.6)
OR CI 95	1 (ref.)	0.93 (0.62–1.40)	*0.54 (0.44–0.66)*
AOR[b] (95% CI)	1 (ref.)	1.53 (0.90–2.61)	0.88 (0.66–1.19)
Start of breastfeeding in the first hour			
No	1302 (24.5)	42 (30.2)	176 (36.2)
Yes	4015 (75.5)	97 (69.8)	310 (63.8)
OR (95% CI)	1 (ref.)	0.75 (0.52–1.08)	*0.57 (0.47–0.69)*
AOR[c] (95% CI)	1 (ref.)	1.13 (0.72–1.78)	0.98 (0.76–1.30)
Newborn admission			
No	4676 (87.9)	117 (84.2)	397 (81.7)
Yes	641 (12.1)	22 (15.8)	89 (18.3)
OR (95% CI)	1 (ref.)	1.37 (0.86–2.18)	*1.64 (1.28–2.09)*
AOR[d] (95% CI)	1 (ref.)	1.10 (0.64–1.87)	1.12 (0.82–1.53)
Exclusive breastfeeding at discharge			
No	1016 (19.1)	37 (26.6)	154 (31.7)
Yes	4301 (80.9)	102 (73.4)	332 (68.3)
OR (95% CI)	1 (ref.)	*0.65 (0.44–0.95)*	*0.51 (0.41–0.62)*
AOR[c] (95% CI)	1 (ref.)	1.01 (0.67–1.52)	0.90 (0.71–1.15)
Composite neonatal morbidity			
No	4191 (79.0)	102 (73.9)	344 (71.1)
Yes	1117 (21.0)	36 (26.1)	140 (28.9)
OR (95% CI)	1 (ref.)	1.32 (0.90–1.95)	*1.53 (1.24–1.88)*
AOR[c] (95% CI)	1 (ref.)	1.20 (0.80–1.80)	1.23 (0.97–1.55)
Postpartum surgery related to delivery			
No	5142 (96.7)	134 (96.4)	451 (92.8)
Yes	175 (3.3)	5 (3.6)	35 (7.2)
OR (95% CI)	1 (ref.)	1.10 (0.44–2.71)	*2.28 (1.57–3.32)*
AOR[e] (95% CI)	1 (ref.)	1.08 (0.43–2.72)	*1.71 (1.10–2.66)*
Postpartum maternal ICU admission			
No	5235 (98.5)	137 (98.6)	459 (94.4)
Yes	82 (1.5)	2 (1.4)	27 (5.6)
OR (95% CI)	1 (ref.)	0.93 (0.23–3.83)	*3.76 (2.41–5.86)*
AOR[e] (95% CI)	1 (ref.)	1.06 (0.25–4.60)	*2.23 (1.26–3.93)*
Re-admission after discharge			
No	5216 (98.1)	137 (98.6)	470 (96.7)

Table 4 (continued)

Variable	Type of conception		
	Spontaneous (*n* (%))	Insemination (*n* (%))	IVF
Yes	101 (1.9)	2 (1.4)	16 (3.3)
OR (95% CI)	1 (ref.)	0.75 (0.18–3.09)	*1.76 (1.03–3.00)*
AOR[e] (95% CI)	1 (ref.)	0.63 (0.15–2.63)	1.17 (0.64–2.16)
Composite postpartum morbidity			
No	4998 (94.0)	130 (93.5)	423 (87.0)
Yes	319 (6.0)	9 (6.5)	63 (13.0)
OR (95% CI)	1 (ref.)	1.09 (0.55–2.15)	*2.33 (1.75–3.11)*
AOR[f] (95% CI)	1 (ref.)	0.97 (0.48–1.95)	*1.94 (1.40–2.69)*

[a] Adjusted by maternal age, BMI, nulliparity, twin pregnancy, previous caesarean, smoking habit, economic income, level of education, nationality, maternity training and pregnancy complications

[b] Adjusted by maternal age, BMI, nulliparity, twin pregnancy, previous caesarean, smoking habit, economic income, level of education, nationality, maternity training and pregnancy complications + newborn weight, prematurity, induced delivery, severe tearing, type of delivery, altered FHR, stained amniotic fluid and newborn admission

[c] Adjusted by maternal age, BMI, nulliparity, twin pregnancy, previous caesarean, smoking habit, economic income, level of education, nationality, maternity training and pregnancy complications + severe tearing, type of delivery, newborn admission and breastfeeding previous children

[d] Adjusted by maternal age, BMI, nulliparity, twin pregnancy, previous caesarean, smoking habit, economic income, level of education, nationality, maternity training and pregnancy complications + severe tearing, type of delivery, altered FHR and stained amniotic fluid and newborn admission

[e] Adjusted by maternal age, BMI, nulliparity, twin pregnancy, previous caesarean, smoking habit, economic income, level of education, nationality, maternity training and pregnancy complications + severe tearing, type of delivery, pregnancy complications, pre-eclampsia, vaginal bleeding during delivery, fever and uterine rupture

[f] Adjusted by maternal age, BMI, nulliparity, twin pregnancy, previous caesarean, smoking habit, economic income, level of education, nationality, maternity training and pregnancy complications + composite pregnancy morbidity and composite delivery morbidity

Italic font indicates statistically significant differencesItalic font indicates statistically significant differences

As to the relationship of the type of conception with the most important sociodemographic and obstetric characteristics, we do not find any statistically significant differences as for nationality and BMI. However, we do find a statistical association with maternal age, level of education, family income level, maternity training attendance, smoking habits before pregnancy, number of pregnancies and previous births. In particular, women with spontaneous pregnancies were younger, had a lower level of education and economic incomes, less usually attended maternity training, had higher pre-pregnancy smoking habits, and a higher number of previous pregnancies and births than the women who underwent IVF. All the details of this analysis can be found in Table 1.

After performing the multivariate analysis, we observed that women undergoing some assisted reproductive technique are more likely to develop complications during pregnancy as shown in detail in Table 2. Pregnancies achieved through IVF were 9.17 times more likely to have a twin pregnancy (95% CI, 6.02–13.96), 1.58 (95% CI, 1.28–2.22) times more likely to have a risk of preterm birth and 1.43 (95% CI, 1.01–2.02) times more likely to have a premature child as compared with spontaneous pregnancies. If we focused on the typical pathologies of gestation, they showed a higher likelihood of hypertensive states (AOR 1.98; 95% CI, 1.44–2.73), gestational diabetes (AOR 1.45; 95% CI, 1.11–1.90) and hypothyroidism (AOR 1.64; 95% CI, 1.27–2.11). No differences were observed regarding the other study variables. By assessing the factors studied as a single variable, composite pregnancy morbidity, we obtain that IVF pregnancies have an overall risk 1.71 times greater than spontaneous pregnancies (95% CI, 1.37–2.13).

Regarding complications during delivery, it was observed that women with IVF have an overall higher risk of complications during delivery, as shown by the variable composite birth morbidity (AOR 1.48; 95% CI, 1.17–1.88), than those who had a spontaneous pregnancy. In particular, they are more likely to undergo an induced birth (AOR 1.46; 95% CI, 1.19–1.80) and complications such as stained amniotic fluid (AOR 1.50; 95% CI, 1.03–2.18), vaginal bleeding (AOR 2.10; 95% CI, 1.46–3.03) and pre-eclampsia (AOR 1.68; 95% CI, 1.03–2.73). When focusing on the type of end of delivery, we get that these women are more likely to end up in an urgent C-section (AOR 1.35; 95% CI, 1.02–1.78) and to suffer III or IV degree tearing (AOR 3.19; 95% CI, 1.66–6.14), as shown by the data on Table 3.

Finally, after performing the analysis of maternal and foetal complications during the postpartum period, we find that women undergoing IVF are more likely to be admitted at the ICU service (AOR 2.23; 95% CI, 1.26–3.93) and to suffer surgeries related to the delivery process (AOR 1.71; 95% CI, 1.10–2.66). In general, we obtain that the composite postpartum morbidity is greater (AOR 1.48; 95% CI, 1.17–1.88) for

mothers undergoing IVF, while if we focus on composite neonatal morbidity (AOR 1.48; 95% CI, 1.17–1.88), we do not get significant differences. The other analysed results were not related to the type of conception, as shown in Table 4.

Discussion

The expansion of assisted reproductive techniques in recent years is undeniable. However, studies relating the use of these techniques with obstetric and perinatal outcomes are limited due to the wide variety of designs, populations and countries. In Spain, in particular, there are few studies in this regard. However, this study has corroborated the increase in complications in this type of gestations, for both pregnancy and delivery and postpartum.

Of the 5942 women participating in the study, 10.5% achieved pregnancy using assisted reproductive techniques. These techniques were divided into two categories. On the one hand, artificial insemination and, on the other hand, in vitro fertilisation. In all the analysed variables, there is a greater likelihood of complications with gestations obtained through IVF as compared with artificial insemination.

Women who underwent IVF to achieve pregnancy had a higher risk of twin pregnancy, risk of preterm birth, prematurity, gestational diabetes, hypothyroidism, stained AF, vaginal bleeding, pre-eclampsia, induced delivery, urgent caesarean section, III–IV tearing, ICU admittance and surgeries related to the delivery process.

One of the most traditionally studied factors is the emergence of pre-eclampsia in gestations achieved through ART, but the results show some controversy. While the Chen et al. study [22] found no evidence of increased risk of pre-eclampsia in pregnancies achieved with artificial insemination, a more recent study published by Zhu et al. [11] observed an increased risk of hypertensive disorders during ART gestations, which is consistent with other studies such as the ones by Chen, Shevell, Jackson and Ashrafi [12, 22–24]. In relation to the data obtained in this study, no increased incidence of hypertensive disorders during pregnancy has been observed, although we have observed an increase in these disorders during delivery in pregnancies conceived by IVF at the moment of delivery. These differences may be due to the results of globally increased blood pressure, without distinction with regard to pregnancy and delivery.

The study by Zhu et al. [11] found a significant increase in the incidence of gestational diabetes in women undergoing ART. This incidence increase was also reported in the studies by Reddy et al. [25], Allen et al. [26] and Kouhkan et al. [6]. In the present study, this result has been corroborated for women who underwent IVF, but not for those who underwent artificial insemination. However, these data are relevant due to the increased risk of developing maternal and foetal complications [7, 27].

In relation to the incidence of intrahepatic cholestasis, this study has found no significant differences regarding women with spontaneous pregnancies. However, the study by Zhu [11] found results that point in the opposite direction, although this may be because this pathology is more prevalent among the Chinese population than in our context. In this sense, it would be interesting to carry out new studies aimed at determining whether intrahepatic cholestasis is more prevalent in women with ART pregnancies.

Where there does seem to be consensus with other studies is in the increased risk of prematurity in this population as compared with women who achieved spontaneous pregnancy.

During the postpartum period, in this study, we have detected an increase in surgical interventions in relation to delivery and ICU admission. We have not however found other studies in which these variables are measured, so we consider it interesting to further research so as to corroborate these data in other contexts.

Among the limitations of the study, we find the possibility of a reporting bias due to the study design, since it is the participants themselves who report on its process and the sourcing participants from lactation associations and postpartum clinics, although our prevalence falls within the range of published studies. We did not ask about the time to pregnancy and thus had no information on this issue. Another limitation is that whether the insemination took place with or without ovarian stimulation has not been taken into account, as what happens with the causes of infertility. This could make a difference in the risk of adverse outcomes. In this case, the authors consider the possibility of an information bias in the participants' answers due to the technical complexity of the questions. In addition, some pathologies were likely to be undervalued as women were asked to state the 'No' option for those assessed pathologies that raised some doubts. The authors chose this option so as to avoid overstating the pathologies as well as to improve the subsequent multivariate analysis through reducing the number of losses for failing to fill in the survey questions.

Among the main strengths of the study, we can highlight the large sample size, this being the study with the largest number of participants conducted in Europe on this topic [28]. While the design of the study may present certain biases, the authors consider that the observed findings may be useful for other researchers to initiate new lines of research, and especially for clinicians to consider the possibility of these complications associated with reproductive techniques towards improving the management of pregnant women and their newborns.

In short, we can consider that pregnancies achieved through IVF show a higher risk of adverse outcomes than those achieved by artificial insemination although the causes of such differences remain unclear.

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