



PRETERM BIRTH AND LOW BIRTH WEIGHT IN SINGLETON PREGNANCIES AFTER IN VITRO FERTILIZATION- INFLUENCE OF INFERTILITY AND METHOD OF FERTILIZATION

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ABSTRACT

The aim of our study was to determine the effect of infertility and the method of fertilization on the frequency of preterm birth and low birth weight in singleton pregnancies achieved by in vitro fertilization (IVF).

The study was conducted in the period 01.2013 - 12.2017 and included 286 patients with births from singleton IVF pregnancies. Classical IVF received 107 patients (group A1) and ICSI fertilization - 148 (group A2). Cases with tubal infertility were 81 (group B1), and 85 were with male infertility (group B2).

In group A1, birth prior to 37 weeks of gestation (w.g.) was found in 33 (30.8%) cases, compared to 26 (17.6%) in group A2 ($p=0.029$). In group A1, birth weight < 2500 g was observed in 27 (25.3%) of cases, and in group A2 - in 17 (11.5%) of cases ($p=0.015$). In group B1, birth prior to 37 w.g. was established in 26 (32.1%) of the cases, compared to 9 (10.6%) in group B2 ($p=0.003$). In group B1 there was birth weight < 2500 g in 19 (23.5%) of patients, compared to 6 (7.1%) in group B2 ($p = 0.009$). The average weight of the newborn and average duration of pregnancy was lower in groups with IVF fertilization and tubal infertility compared to ICSI fertilization and male infertility.

Tubal infertility and classical IVF fertilization are independent risk factors that increase the frequency of preterm birth and low birth weight in IVF singleton pregnancies.

Keywords: IVF, ICSI, preterm birth, low birth weight, tubal infertility, male infertility,

INTRODUCTION

The use of assisted reproduction methods is constantly increasing worldwide, reaching 5% of newborns in some countries. Many studies have found an increased incidence of preterm birth (PTB) and low birth weight (LBW) in IVF singleton pregnancies [1-3]. These problems are essential for clinical practice, as they determine the

incidence of neonatal morbidity and mortality [4]. Many factors may be related to the outcome of the in vitro fertilization procedure, such as the woman's age and the associated reduction in ovarian reserve [5-7]. A number of studies have found a connection between the type of infertility - tubal or male, and the type of fertilization in IVF - classical IVF or ICSI and the frequency of preterm birth and low birth weight. Some authors believe that the characteristics of women with infertility play a greater role in the increase of risk of LBW than the IVF procedure itself [8, 9]. The aim of the present study was to be determined the incidence of PTB and LBW in singleton IVF pregnancies, depending on the fertilization technique and the type of infertility. Additionally, the average duration of pregnancy and the average birth weight of the fetus in the different study groups were studied.

MATERIALS AND METHODS

The study was prospective and retrospective and was conducted at the University Hospital “Maichin Dom”, Sofia in the period 01.2013 -12.2017 and included a total of 286 births from singleton pregnancies after IVF. Inclusion criteria were: singleton pregnancy at the time of birth, available data for the method of conception (spontaneous or IVF), pregnancy ended with birth later than 22 w.g. and/or fetal weight at birth > 600 g. Exclusion criteria were: preeclampsia, diabetes, placenta previa, placental abruption, previous preterm birth, surgery shortening uterine cervix, inflammatory kidney diseases and anemia. These are risk factors for preterm birth without relation to the method of conception. The main studied indicators were the frequency of preterm birth and low birth weight, the average duration of pregnancy and average birth weight.

Subgroups were formed according to: method of fertilization- 107 cases with IVF fertilization (group A1) and 148 cases with ICSI fertilization (group A2); type of infertility - 81 cases with tubal infertility (group B1) and 85 cases with male infertility (group B2).

Tubal infertility was diagnosed by laparoscopy and/or hysterosalpingography, which revealed damage or obstruction of the fallopian tubes. The male factor of infertility was found during sperm analysis and deviation in the studied indicators according to WHO criteria. We defined preterm birth as birth of a fetus before the end of the 37th, w.g. (259 days from the date of last menstrual period (LMP). Low birth weight was defined as a fetus with weight < 2500 g. at birth. Gestational age was calculated based on LMP and/or the date of embryo transfer. In the absence of data on LMP, gestational age was determined by ultrasound after hospitalization or by morphological criteria after birth. The weight of the newborn is

determined immediately after birth by measuring with an accuracy of 10 g.

Statistical analysis was performed using the SPSS for Windows, v 13. Statistical methods used include descriptive statistical analysis. Mann-Whitney test was used for continuous variables. The counting data were represented by n (%), and χ^2 test were used for categorical variables. At $p < 0,05$ was established statistical significance.

RESULTS

The results regarding incidence of preterm birth and low birth weight according to the type of fertilization in the IVF cycle are shown in Table 1.

Table 1. Gestational age and birth weight according to the type of fertilization - IVF or ICSI.

Indicator		IVF n (%)	ICSI n (%)	Total n (%)	p
Gestational age	> 37 w.g.	74 (69.2)	122 (82.4)	196 (76.9)	0.029
	32-37 w.g.	23 (21.5)	21 (14.2)	44 (17.3)	
	< 32 w.g.	10 (9.3)	5 (3.4)	15 (5.9)	
Birth weight	> 2500 g.	80 (74.8)	131 (88.5)	211 (82.7)	0.015
	1500-2500 g.	22 (20.6)	13 (8.8)	35 (13.7)	
	< 1500 g.	5 (4.7)	4 (2.7)	9 (3.5)	

The average weight of the newborn in group A1 was 2863.36 g. compared to 3117.84 g. in group A2 ($p < 0.001$). A shorter duration of pregnancy in the group A1 was observed (257.69 days) compared to that in group A2 (265.69 days). The difference averaged 7.56 days and was statisti-

cally significant ($p = 0.005$).

The results regarding incidence of preterm birth and low birth weight according to the type of infertility are shown in Table 2.

Table 2. Gestational age and birth weight according to the type of infertility - tubal or male.

Indicator		Tubal infertility n (%)	Male infertility n (%)	Total n (%)	p
Gestational age	> 37 w.g.	55 (67.9)	76 (89.4)	131 (78.9)	0.003
	32-37 w.g.	20 (24.7)	6 (7.1)	26 (15.7)	
	< 32 w.g.	6 (7.4)	3 (3.5)	9 (5.4)	
Birth weight	> 2500 g.	62 (76.5)	79 (92.9)	141 (84.9)	0.009
	1500-2500 g.	16 (19.8)	4 (4.7)	20 (12)	
	< 1500 g.	3 (3.7)	2 (2.4)	5 (3)	

The average weight of the newborn in group B1 was 2841.36 g. compared to 3181.65 g. in group B2 ($p < 0.001$). There was also a shorter duration of pregnancy in women in group B1 compared to group B2 - 258.52 days vs 266.35 days. The difference averaged 7.83 days and was statistically significant ($p < 0.001$).

DISCUSSION

Our study found almost twice the increased incidence of preterm birth and more than twice the increased incidence of low birth weight in patients with classical IVF fertilization compared to those with ICSI fertilization.

The birth weight was lower by an average of 254 g., and the duration of pregnancy was lower by an average of 7.56 days in patients receiving classical IVF compared to those with ICSI. ICSI has become the most commonly used technique over the years, even in the absence of a male factor for infertility. The method has different advantages and disadvantages [10]. Following the introduction of the method into clinical practice in 1992 by Palermo et al. [11], some scientists have expressed concern that it may have a negative effect on the course of pregnancy and the newborn [12, 13]. Numerous authors compared the outcome of pregnancy when different types of fertilization

were performed - classical IVF or ICSI. Pinborg A, et al. [14] in their large meta-analysis found a lower risk of PTB and LBW in ICSI singleton pregnancies compared to pregnancies achieved by classical IVF. This may be due to the fact that couples treated with ICSI are predominantly with male factor, and mothers are not affected by infertility [15]. Other authors reach similar conclusions by establishing a lower incidence of preterm birth and low birth weight in pregnancies achieved by ICSI fertilization [16]. A large study of 3974 singleton births after IVF and 1655 singleton births after ICSI found that IVF and ICSI singleton pregnancies had a similar course in obstetric and perinatal complications. The only significant difference is the higher risk of birth <37 weeks of gestation in IVF pregnancies compared to those with ICSI - 12.4% vs 9.2% [17]. There is a possibility that oocyte quality may affect the success rate and outcome of pregnancy in infertile women [18].

Tubal infertility is one of the most common causes of infertility - about 30-35% of all cases and is associated with a higher incidence of preterm birth and low birth weight in singleton pregnancies achieved by IVF. A large study in the United States found that the incidence of preterm birth in IVF singleton pregnancies with tubal fac-

tor was 15.8% compared to 11.6% in male infertility factor. The risk of preterm birth is higher at all stages of pregnancy. The risk of giving birth to low and very low birth weight neonates is also higher [19]. These conclusions are supported and by other authors [16, 20]. Our study found a 3-fold higher frequency of preterm birth and a 3.3-fold higher frequency of low birth weight in patients with tubal infertility compared to those with a male infertility factor. The observed average weight of the newborn in patients with tubal infertility was 230 g. lower, and the average duration of pregnancy was about 8 days shorter than the results in patients with male infertility factor.

CONCLUSION

According to the results of our study, tubal infertility and the classical in vitro fertilization are an independent risk factor that increases the frequency of preterm birth and low birth weight in singleton pregnancies achieved by in vitro fertilization. The obtained results also support the growing practice in the clinics of assisted reproduction for using the ICSI technique, regardless of the cause of infertility, as a safer way both in terms of fertilization and for the pregnancy outcome.

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