ASSESSMENT OF FETAL WEIGHT COMING FROM PREGNANCIES OBTAINED BY IN VITRO FERTILIZATION - CASE CONTROL STUDY

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Keywords: *IVF, weight, pregnancy, fetus, group*

Abstract: *One of the most discussed topics in the current literature is the influence of human assisted reproductive techniques (ART) on fetal growth. Numerous studies have been conducted to determine the factors that influence the fetal weight of newborns achieved through ART. It has come to the theory that the weight of newborns obtained by ART is influenced by several factors: the expression of genes influenced by ovarian stimulation, the impact on genome expression at the endometrial level, placental development and placental weight, complications of pregnancy, age of sterility, and ART indications. The aim of the study is to assess the weight of IVF newborns. We also evaluated the delivery path, the presentation and other associated pathologies of the fetuses. We conducted a statistical, retrospective and comparative study. The study was conducted on a group of 106 patients from pregnancies obtained by in vitro fertilization (IVF).The study included patients from the Emergency County Clinical Hospital of Sibiu, Obstetrics and Gynecology Clinic from January 2010 to December 2016. The IVF group was compared to a control group of 212 patients. Concidering the small number of cases we selected two witnesses for each patient. Depending on gestational age, birth weight, waist, cranial perimeter, weight index, Apgar score at 1 minute, physiological weight loss and duration of hospitalization - there were no differences with statistical significance between the two groups. In the IVF group 63.2% of the patients were female compared to the control group where only 44.3% of the patients were female. There are no significant differences in the weight of the patients between the IVF group and the control group.The weight ratio of newborns within the IVF group has a value close to that of newborns in the control group. There are no statistical differences between the IVF group and the control group regarding waist and cranial perimeter.*

INTRODUCTION

Fetal weight is the main indicator of normal pregnancy evolution.

The most common maternal pathologies associated with abnormal fetal growth are unbalanced diabetes mellitus associated with fetal weight gain and cardiovascular disease complicated with intrauterine growth restriction /small for gestational age.(1,2,3)

Although fetal weight is an indicator of well-being in utero, its variations without alteration of other parameters do not indicate a complication of pregnancy.(4)

One of the most discussed topics in the current literature is the influence of human assisted reproductive techniques (ART) on fetal growth.

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It has come to the theory that the weight of newborns obtained by ART is influenced by several factors: the expression of genes influenced by ovarian stimulation, the impact on genome expression at the endometrial level, placental development and placental weight, complications of pregnancy, age of sterility, and ART indications.(5,6,7,8)

Newborn in the US that come from IVF pregnancies have a lower birth weight than those naturally conceived without a causal link due to maternal age, parity, or gestational age at birth (136.972 pregnancies).

A comparative analysis shows a higher frequency of premature births in IVF pregnancies.

The intimate mechanism of small weight at birth is still unknown.

Use of HMG - associated with significant increases in insulin growth factor-binding protein 1 is related to intrauterine growth retardation.

IVF pregnancies have different endometrial gene expression with modified endometrial protein levels and increased placental structural abnormalities.

An explanation for lower birth weight is elective cesarean before term.

For fetal pregnancies designed by ART, there are no significant differences with those naturally conceived - multiple pregnancies are already a significant risk.(9)

In the Netherlands, a case control study was carried out at 4 university clinics.

The study included 307 pregnancies obtained through IVF and 307 pregnancies obtained spontaneously. In IVF pregnancies, labor was established 3 days earlier compared to spontaneously obtained pregnancies (275 versus 278 days, P = 0.05).

The number of newborns, small for gestational age was higher in the IVF pregnancy group compared to the newborns from spontaneous pregnancies (16.2 versus 7.9%, P <

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Article received on 28.01.2017 and accepted for publication on 26.02.2018
ACTA MEDICA TRANSILVANICA March 2018;23(1):77-80

0.001).(10)

A comparative analysis of IVF and intracytoplasmic sperm injection (ICSI) pregnancies showed that the incidence of prematurity was higher in neonates from ICSI (31.8%) compared to those born from IVF (29.3%). Very low birth weight is more common in IVF pregnancies (5.7%) compared to ICSI (4.4%).

Major malformations (defined as major dysfunctions requiring surgical corrections) were observed in 3.4% for ICSI pregnancies and 3.8% for those obtained with IVF (P = 0.538).

Intrauterine fetal death (before 20 gestational weeks) was 1.69% in the ICSI group versus 1.31% in the IVF group.

The overall incidence of malformations (the severe ones associated with fetal intrauterine death, with those in the abortion and from live births) was 4.2% for the ICSI group and 4.6% for the IVF group (P = 0.482).(11)

The development of IVF fetuses remains a highly discussed topic in the literature. Numerous studies have been conducted on fetal development depending on the culture medium used in embryo culture.

A study was carried out which aimed to assess the growth in the first two years of life of children from IVF pregnancies in two Vitrolife and Coook culture. The study included 265 children, of which 117 were from Cook culture, and 148 on Vitrolife culture.

The study found that there were significant differences between the two groups in terms of both weight and length. Children from embryos cultivated on the Vitrolife culture are heavier (p = 0.005) and taller (p = 0.031) in the first two years of life.(12)

A Swedish study over a 5-year period that included 1293 ART pregnancies shows that the mean weight of fetuses from ICSI single pregnancy and cryopreservation is higher than that of fetuses from single embryo transfer (ET) fresh pregnancies.(13)

As the difference in the growth of fetuses coming from IVF pregnancies from different culture medium became a reality, the question arises as to when change occurs in intrauterine growth of embryos grown on different culture.

A study that included 294 single IVF pregnancies, of which 168 on the Vitrolife medium and 126 on the Cook medium, show that there are no differences in embryonic growth in the first trimester of pregnancy.

However, from 20 weeks of gestation, the assessment of biometric parameters: biparietal diameter, head circumference and trans-cerebellar diameter show a significant increase in Vitrolife group versus Cook group -head circumference in the Vitrolife group head (HCvl) 177.3 mm, circumference in the Cook group (HCc) 175.9 mm, adjusted mean difference 1.8, *P* = 0.03; trans cerebellar diameter in the Vitrolife group (TCDvl) 20.5 mm, trans cerebellar diameter in the Cook group (TCDc) 20.2 mm, adjusted mean difference 0.4, *P* = 0.008).(14)

PURPOSE

In the literature, in the IVF pregnancies, weight changes, such as: fetal macrosomia or intrauterine growth restriction were observed.

The aim of the study is to assess the weight of IVF newborns. We also evaluated the delivery path, the presentation and other associated pathologies of the fetuses.

MATERIALS AND METHODS

We conducted a statistical, retrospective and comparative study. The study was conducted on a group of 106 patients obtained by in vitro fertilization (IVF).

The study included patients from the Emergency County Clinical Hospital of Sibiu, Obstetrics and Gynecology Clinic from the period January 2010 to December 2016.

The IVF group was compared to a control group of 212 patients. Considering the small number of cases we selected two witnesses for each patient.

The inclusion criterion for patients in the study was: to be live newborns obtained by in vitro fertilization from singleton or multiple pregnancies within seven years, and compared with the control group, including spontaneous pregnancies – with patients of the same age.

The gestational age was objectively established in postpartum by Ballard score by the neonatology team.

The characteristics that were considered in the study were: gender, environment, year of birth, birth weight, gestational age, waist, cranial perimeter, weight index, singleton or twin pregnancy, spontaneous of IVF pregnancy, vaginal/vacuum, cesarean, cranial pelvic/transverse presentation, Apgar score, trauma at birth, infections, jaundice accentuated, congenital anemia, persistence of fetal circulation with arterial and foramen oval persistence, associated pathologies, physiological weight loss, birth feeding - natural, artificial or mixed, number of days of hospitalization, respiratory distress syndrome.

For statistical analysis we used the program for statistical calculation SPSS for Windows 10.0; statistical tests t-test and Chi-square.

P was considered statistically significant at values <0.05.

The confidence interval was 95%.

RESULTS

Depending on gestational age, birth weight, waist, cranial perimeter, weight index, Apgar score at 1 minute, physiological weight loss and duration of hospitalization - without differences with statistical significance between the two groups (table. no 1).

Table no 1. General data of the studied groups

	IVF GROUP	CONTROL GROUP	P
Gestational age (weeks)	37,62 ±1,70	37,62 ±1,69	1,000
Birth weight (g)	2892,17 ±597,03	2930,57±554,94	0,571
Length (cm)	50,96 ±3,24	51,38 ± 3,03	0,261
Cranial perimeter (cm)	33,03±1,76	36,72±3,33	0,256
Weighted index	2,14 ±0,15	2,13 ±0,19	0,533
Apgar score 1’	9,47± 0,78	9,34 ±0,94	0,207
Physiological weight loss (g)	181,04 ± 52,84	172,49 ±57,29	0,199
Duration of hospitalization (days)	6,94±7,41	7,11±10,13	0,881

In the IVF group, 63.2% of the patients were females compared to the control group, where only 44.3% of the patients were females. 72.2% of patients in the IVF group come from the urban environment and only 27.8% from the rural environment - the environment plays an important role in the socio-economic level as well as the level of education of the patients.

In the control group, 65,6% of the patients come from the urban environment and 34,4% from the rural environment.

93.4% of patients in the IVF group were born via cesarean section and 6.6% were vaginal births- no forceps was applied.

In the control group, 56.6% of patients were born vaginally, of which 9% by forceps application and 42.5% by cesarean section.

The indications for cesarean section birth in the IVF group were: IVF pregnancy 55.5%, old for the first pregnancy 14.4%, twin pregnancy 9.8%, prior Cesarean section7.2%, pelvic presentation 3.9%, thrombophilia 3.7%, placenta praevia 1.1%, negative labor test 1.1%, cardiac pathology 1.1%, acute fetal distress 1.1% (table no 2).

Our study shows an increased Cesarean section delivery rate of pregnancy obtained through IVF. Both in the IVF group and in the control group, most of the fetuses were placed in the cranial presentation at the time of birth – 80% in the IVF group and 85% in the control group.

Cephalic bosa was the most common birth trauma in both groups, followed by bruising and clavicle fractures.

In the IVF group, 60% of the patients presented the cephalic bosa and in the control group 48,8%. There is a difference of about 12% between the two groups.

26.7% of the patients in the IVF group had bruising at birth and 39.1% of the patients from the control group.

13.3% of the newborns from the FIV group had clavicle fracture at birth and only 2.4% of the newborns in the control group had clavicle fracture at birth.

5.7% of patients in the IVF group experienced amniotic infections, and in the control group, 4.2% of patients experienced amniotic infections.

Arterial canal persistence is 5.7% for both groups.

Foramen oval persistence is higher in the control group compared to the IVF group. 21.2% of patients in the control group experienced foramen oval persistence while only 13.2% of patients in the IVF group experienced foramen ovale persistence. 72.6% of patients in the IVF group experienced jaundice accentuated, and 68.7% from the patients from the control group.

10.4% of patients in the IVF group had congenital anemia and 6.1% of the patients in the control group.

Table no. 2. Indications of caesarean section in the IVF group compared to the control group

Indication for caesarean section	IVF GROUP	CONTROL GROUP
IVF	55,5%	0%
Old for the first birth	14,4%	7,8%
Twin pregnancy	9,8%	26,3%
Negative labor test	1,1%	5,6%
Prior caesarean section	7,2%	32,2%
Pelvic presentation	3,9%	3,9%
Important myopia	0%	3,3%
Placenta praevia	1,1%	2,2%
Thrombophilia	3,7%	2,2%
Infection with HVB	0%	2,2%
Thrombocytopenia	0%	1,1%
Cardiac pathology	1,1%	4,4%
Fetal distress	1,1%	2,2%
Congenital hip dislocation	0%	1,1%
Unique kidneys	0%	1,1%
Hydrocephaly	0%	1,1%
Heart failure	0%	1,1%
Spontaneously broken membranes	1,1%	1,1%
Umbilical cord prolapse	0%	1,1%

DISCUSSIONS

Our study showed that in our clinic, as in other clinics, the cesarean delivery rate for pregnancies obtained through IVF is high. Certainly, an important role is played by the mental component on both the mother and the obstetrician.

An important component is the advanced age of women who have had a pregnancy through IVF.

Our study also highlights the importance of the educational and socio-economic level of patients. Most women who have a pregnancy through IVF come from the urban environment and have higher education.

Regarding the predominance of female girls coming from IVF pregnancies, there are no data showing that preimplantion tests have been performed in that matter.

CONCLUSIONS

There are no significant differences in the weight between the IVF group and the control group.

The weight ratio of newborns within the IVF group has a value close to that of newborns in the control group.

There are no statistical differences between the IVF group and the control group regarding waist and cranial perimeter.

There is a significant gender difference - in the IVF group most children are female and in the control group most of the children are male.

It has been observed that most of the patients in the IVF group were born via caesarean section, unlike those in the control group, which are significantly fewer.

In-vitro fertilization pregnancies are the most common indication of cesarean section in the IVF group, and in the control group the most common indication of cesarean section is prior cesarian section.

Both in the IVF group and in the control group, most of the fetuses were placed in the cranial presentation at the time of birth.

Bosa cephalic was the most common birth trauma in both groups, followed by bruising and clavicle fractures.

There are no significant differences between the two groups for: neonatal infections, respiratory distress, congenital anemia, neonatal jelly, arterial canal persistence, foramen oval persistence and incidence of malformations.

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