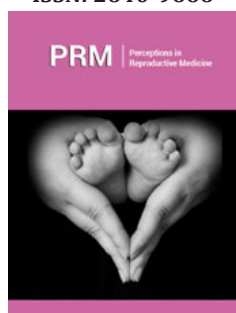


Birth Weight and Neurodevelopment Outcome in Singleton Babies: A Comparison between Assisted Reproductive Techniques and Control Group

ISSN: 2640-9666



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Submission: 📅 January 27, 2023

Published: 📅 February 17, 2023

Volume 5 - Issue 4

How to cite this article: Mahbod kaveh, Zahra Kaveh, Tanha FD*, Roya hamrahi, Mahboubeh shirazi, Maryam veisizadeh, Mamak shariat and Zahra shahraki. Birth Weight and Neurodevelopment Outcome in Singleton Babies: A Comparison between Assisted Reproductive Techniques and Control Group. *Perceptions Reprod Med.* 5(4). PRM. 000617. 2023. DOI: [10.31031/PRM.2023.05.000617](https://doi.org/10.31031/PRM.2023.05.000617)

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Abstract

Objective: This study examined the birth weight of singleton babies born after assisted reproductive techniques and their neurodevelopment outcome until the sixth month of birth in comparison with the singleton babies born without infertility treatment.

Study design: Prospective case-control study

Setting: University-based hospitals. four hundred patients were enrolled in the study. Two hundred were in control group without infertility and two hundred with infertility treatment as case group

Main outcome measure(s): mean weights at birth, at the third and the sixth month and developing.

Examination results: The mean Birth Weights (BW) of infants of the case group and those infants of the control group were $2998.97g \pm 305.93$ and $3245.82g \pm 414.58$ respectively. The difference between groups was statistically significant ($p=0.001$). Neurodevelopment delay occurred in infertility group, like the ability to recognize bottle and breast at the third month and the ability to reach the mouth by the leg and roll and sit alone at the sixth month. It seems that lower birth weight is associated with some retardation in neurodevelopment function of infertility group's infants.

Conclusion: Singleton pregnancy infants who were born after assisted reproductive techniques had lower birth weight than those without background of infertility treatment. This difference may have some effects on their neurodevelopmental ability.

Keywords: Birth weight; Neurodevelopment outcome

Introduction

Infertility is defined as the failure to have pregnancy after one year of regular Intercourse without contraception [1]. Poor obstetrics outcomes are common in babies born after assisted reproductive technologies. Infertility or treatment for poor pregnancy outcome is not clear. Babies who were born with low- or very low- birth weights had a higher risk of neonatal mortality [2]. Infants born after In Vitro Fertilization (IVF) are lighter than those born after frozen-embryo transfer [3]. Actually, these neonates are large at gestational age in comparison to naturally conceived babies. All types of reproductive methods increase the

risk of still birth [4] preterm labor and low birth weight was seen in Infertile couples who conceive a baby after one year [5-15]. Authors concluded that babies born after Intra-Cytoplasmic Sperm Injection (ICSI) with extracted or ejaculated testicular sperm with extreme Oligoasthenospermia show no sign of developmental problems and their clinical outcome is the same [10]. This study examined the birth weight of singleton babies born after assisted reproductive technologies and their neurodevelopment outcome until the sixth month of birth in comparison with the singleton babies born without infertility treatment.

Methods and Materials

This is a prospective case-control study. Infertile and fertile women were enrolled in the study since March 2011 until February 2014 from two university-based hospitals. The study was approved by the ethical committee of Tehran University of Medical Sciences and all participants signed the informed consent before entering the study. Inclusion criteria for the case group included ages 18-40, first singleton pregnancy, gestation age of below thirty-five weeks, no background of underlying disease or diabetes and preeclampsia, a background of one year or more of infertility for those who had pregnancy with assisted reproductive techniques. The control group had the same criteria except infertility. Four hundred patients were enrolled in the study. Two hundred were in the control group without infertility and two hundred with infertility treatment as case group. The following factors were taken in consideration in this article: age and Body Mass Index (BMI) of mothers, background of miscarriage, duration of infertility, type of assisted reproductive techniques, background of polycystic ovarian syndrome, endometriosis, male factor infertility, type of pregnancy

termination, gestational age, infant gender, birth weight and height, APGAR score, days of Neonatal Intensive Care Unit (NICU) admission, head circumference at birth and three and six months after that and evaluation of neurodevelopment by Developmental Diagnosis-Normal and Abnormal Child Development-Clinical Methods and Pediatric Applications (Gesell and Amatruda1941). The qualitative variables were analyzed using Chi 2 and student's T-test was used to analyze the quantitative data. (CI=95%; P<0.05) The data were analyzed using SPSS18.

Result

The mean Birth Weights (BW) of infants in the case and control groups were 2998.97g±305.93 and 3245.82 g±414.58 respectively. The difference between groups was statistically significant (p=0.001). The mean Birth Heights (BH) of infants in the case group and those in the control group were 48.47cm±2.38 and 49.61cm±2.31 respectively. The difference between groups was statistically significant (P=0.001) The mean weights of infants three months after birth were 5689.11g ±880.34 and 6107.82 g±896.47 in case and control groups respectively (p=0.003). The mean head circumferences at birth in the case and the control group were 34.87cm±1.6 and 34.8cm±1.51 respectively. Three and six months after birth, the mean head circumferences in the case group were 40.39cm±2.28 and 44.02cm ±2.55 respectively; and in the control group, the mean head circumferences at the third and the sixth month of birth were 40.48±1.94 and 43.71±2.37 respectively. The differences between head circumferences at birth, at the third and the sixth month were not statistically significant between groups (p=0.672).

Table 1: Results of the weight, height and head circumference at birth and three and six months after birth.

	Case Group	Control Group	P Value
Weight (g)			
At birth	2998.97±305.93	3245.82±414.58	0.001
Third month	5689.11±880.34	6107.82±896.47	0.003
Sixth month	7313.82±732.58	7610.17±1006.43	0.001
Height (cm)			
At birth	48.47±2.38	49.61±2.31	0.001
Third month	57.64±2.96	58.31±3.28	0.036
Sixth month	63.22±2.28	64.31±3.69	0.002
Head circumference(cm)			
At birth	34.87±1.6	34.80±1.51	0.636
Third month	40.39±2.28	40.48±1.94	0.672
Sixth month	44.02±2.55	43.71±2.37	0.212

Case Group: infertile group; Control Group: fertile group

The results are reported as mean ± SD; P<0/05 is statistically significant

Table 2: Third month neurodevelopment outcome.

	Case Group	Control Group	P Value
Third month			
Ability to laugh	42.40%	57.60%	0.708

Ability to hold the neck	41.60%	58.40%	0.158
Ability to react to the sounds	42.20%	57.80%	0.257
Ability to look directly to the objects	42.70%	57.30%	0.223
Ability to recognize bottle and breast	41.60%	58.40%	0.004

Case Group: infertile group; Control group: fertile group

The results are reported as frequency (percentage); $P < 0/05$ is statistically significant

Table 3: Sixth month neurodevelopment outcome.

	Case Group	Control Group	P Value
Sixth month			
Ability to put objects in the mouth	42.20%	57.80%	0.99
Ability to reach the mouth by the leg	39.90%	60.10%	0
Ability to roll	39.30%	60.70%	0
Ability to sit alone	38.40%	61.60%	0.001
Ability to give objects by the hand	42.60%	57.40%	0.099

Case Group: infertile group; Control group: fertile group

The results are reported as frequency (percentage); $P < 0/05$ is statistically significant

Table 1 shows the result of the weight, height and head circumference at birth and three and six months after birth. The ability to laugh and hold the neck ($p=0.158$) and react to the sounds ($p=0.162$) and look directly to the objects ($p=0.223$) at the third month was the same in both groups. The ability to recognize bottle and breast ($p=0.004$) was different at the third month in the two groups. But after six months, both groups' babies acted similarly in to recognize bottle and breast. The ability to put objects in the mouth at the sixth month was the same in the two groups. However, at the sixth month, the ability to reach the mouth by the leg and roll and sit alone had retarded in the infertility group compared to the control group ($p=0.001$), but the ability to give objects by the hand was the same in both groups ($p=0.09$). Table 2 & 3 show neurodevelopment outcome The head circumferences at birth in Intrauterine Insemination (IUI) and ICSI groups were 35.26 ± 1.29 cm and 34.5 ± 1.68 cm respectively; the difference was statistically significant ($p=0.001$).

The mean birth heights in IUI and ICSI groups were 48.22 ± 1.87 cm and 48.69 ± 2.92 cm respectively. ($p=0.178$) The birth weights in IUI and ICSI groups were 3019.75 ± 275.76 g and 3003.5 ± 363.8 g respectively. ($p=0.716$) The mean birth heights in IUI and ICSI groups at the third month were 57.09 ± 2.59 cm and 57.93 ± 3.5 cm respectively ($p=0.055$). The mean head circumferences at the third month were 40.63 ± 1.76 cm and 40.21 ± 2.68 cm respectively. ($p=0.198$) The mean weights at the third month in IUI and ICSI groups were 5864.5 ± 811.88 g and 5489 ± 933.37 g respectively ($p=0.003$). The mean heights at the sixth month in IUI and ICSI groups were 62.57 ± 2.59 cm and 63.93 ± 3.29 cm ($p=0.001$). The mean head circumference at the sixth month in IUI and ICSI groups were 44.25 ± 2.38 cm and 44.01 ± 2.12 cm respectively ($p=0.542$). The mean weights at the sixth month in IUI and ICSI groups were 7397.5 ± 590.68 g and 7236.5 ± 907.54 g respectively ($p=0.139$).

Discussion

Some neurodevelopment delay occurred in infertility group, like the ability to recognize bottle and breast at the third month and the ability to reach the mouth by the leg and roll and sit alone at the sixth month. Several studies have been carried out on the birth weights of singleton pregnancy infants after infertility treatment. Authors (2011US) did researches on 1264 women without and 461 women with background of infertility and singleton pregnancy and reported that infants of the infertility group were lighter than the others, but there were no Information infants' heights or head circumferences or neurodevelopment [11].

It seems that lower birth weight is associated with some retardation in neurodevelopment function of infertility group's infants. In this study, birth weight and developing examination of mothers with singleton pregnancy after infertility treatment and those without infertility treatment had been developed. There were four hundred infants divided into two groups. The mean birth weight and those of the third and the sixth months in the case group were lower than those in the control group and the differences were statistically significant.

In study on 16748 infertile women, 920 cases were under assisted reproductive techniques treatment; 904 cases underwent medical treatment and 14673 cases received no treatment. Infants of the ART group were reported to be at a higher risk of poor obstetric outcomes like low-and very low birth weight [12]. In a study, on low birth weight and preterm labor in 144018 mothers (in vitro fertilization cycles) it was demonstrated the risks of low birth weight and preterm labor were higher in women who used donated cycles [13]. In our study, it was demonstrated that mean birth height and those of the third and the sixth months in the case group were lower than those in the control group and

the differences were statistically significant. However, the head circumferences were similar at birth and at the third and the sixth months. In our study, it was demonstrated that examination of birth heights and weights of the infants of both groups showed that the height and weight growths of infertile mothers' infants were lower than the ones of the other group's infants at birth, at the third and at the sixth month.

On the other hand, the quality of movements in three-month-old infants born of mothers with background of infertility is lower than those of fertile mothers [16]. Stromberg's research examined 5,680 babies born by IVF and 11,360 babies conceived naturally and reported that the risk of neurological disability requiring rehabilitation was higher in the ART group [17] in one study, 81 babies born by the ART methods with 85 babies born by naturally conceived pregnancies and found that the minor neurological dysfunction is more likely in the ART group [18]. Everything that disturbs the growth of the neonate, causes weight loss and if continues, results in short stature, and at the end, affects the head circumference. At this study, the infertility group's infants had lower weights and the differences at the statures were significant. Revealed growth retardation, preterm birth, cerebral palsy in one year in infants attributed to the ART induced pregnancies [19] and also, IVF babies got lower scores on a test of moving quality than the natural group babies [20]. Kelly-Vance L et al. [21] reported lower psychomotor development in children born by ART than in naturally conceived children [21]. Some studies reported that IVF risk of neurological and behavioral development problems in the first year of life [22,23] the treatment of this condition causes is not clear, but regarding the etiology, retardation effect can be happened until sixth month.

Conclusion

However, the difference between head circumference growth was not significant. Neurodevelopmental abilities like grasping, recognizing bottle and breast, reaching the mouth by the leg, putting objects in the mouth and reacting to sounds had significant differences in the two groups, whereas other abilities did not differ significantly. However, the ability to sit alone was different at the sixth month and needed to be examined at the ninth month. Singleton pregnancy infants who are born after assisted reproductive techniques are lighter at birth than those without background of infertility treatment. This difference may have some effects on their neurodevelopmental ability. We recommend a large study with longer follow-up duration for examining this aspect of infant development for babies who are born after assisted reproductive techniques. Conflict of interest: There is no conflict of interest in this study. All authors have contributed significantly.

Acknowledgement

This study was sponsored by deputy research of Tehran University of Medical Sciences

We have financial support of Tehran University of Medical Sciences (tums).

This article is part of thesis for Roya Hamrahi(number:21697), students of general practitioner in medical faculty in TUMS of Iran.

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