Original Article

Comparison of Growth Parameters of 5-year-old Singleton Children Born in Assisted Versus Natural Conception

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Abstract

Introduction: At present, about 1% of newborns are delivered through assisted reproductive technologies (ART) worldwide. This study aimed to evaluate and compare the growth parameters of children born in assisted and natural conception at 5 years of age. Materials and Methods: In a cross-sectional case control study, weight, height and head circumference of 5-year old children were assessed. The case group consisted of term, singleton babies who were products of ART in the Center for Infertility of Shahid Sadoughi University, Yazd, Iran in 2005. The control group consisted of term, first child, singleton and spontaneously conceived 5-year-old children who were referred for vaccination to primary health care center of Shahid Akbari in 2010. Results: Fifty-eight girls (47.5%) and 64 boys (52.5%) "with equal numbers in each of the 2 groups" were evaluated. Sex distribution, mean ages of fathers and mothers were not statistically significant different in both groups. Children born after ART tend to have lower birth weight, smaller birth head circumference and lower weight at 5 years of age. Having low birth weight (<2500 g), being underweight and having short stature at the age of 5 were more common in babies born through ART. Conclusion: Growth retardation is more prevalent in babies born through ART. Thus, growth assessment, parents' knowledge about child physical development, and timely and accurate follow-up of these children are necessary for early detection of any growth disorders.

Ann Acad Med Singapore 2013;42:80-4

Key words: ART, Growth, Height, Natural Conception, Weight

Introduction

The first successful birth resulted from in-vitro fertilisation (IVF) was reported in 1978.[1] Today this technology is being used worldwide and currently, approximately 1% of live births of the world are conceived via assisted reproductive technologies (ART), which include IVF and intracytoplasmic sperm injection (ICSI).[2]

About 10% to 15% of couples have difficulty in conceiving, or have less than the desired number of children and are therefore seeking infertility treatment at least once in their reproductive lifetime.[3]

The prevalence of infertility, defined as failure in pregnancy after 1 year of unprotected intercourse, was reported as 4.9% to 6.1% in the Yazd Province, Iran.[4]

Increase in incidence of caesarean deliveries, perinatal mortality, autosomal and sex chromosome abnormalities, congenital malformations, multiple gestation pregnancies and premature deliveries have been reported in ART conceptions by some studies.[5,6]

It seems that majority of these complications are related to the increase in incidence of multiple gestations. Although ART and natural conception multiple pregnancies appear to have similar outcomes, singleton ART deliveries are however associated with an increased incidence of complications.[7]

Progress and promotion in these methods of pregnancy induction have led to an increase in the number of neonates

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born through ART resulting in some concerns about the outcomes of these children. The use of hormonal drugs during pregnancy and embryo manipulation (ICSI, zona reduction etc) methods in conceptions by ART may affect the long-term health of children conceived through ART.[8]

Little is known, however, about the postnatal growth of ART newborns. The purpose of this study was to evaluate and compare growth parameters (weight, height and head circumference) of 5-year-old ART conceived children born in Yazd, central city of I.R. Iran with those from spontaneously conceived pregnancies.

Materials and Methods

In a cross-sectional case control study, based on Z formula and confidence interval of 95% with 80% power to detect a 20% difference in frequency of growth disorders between groups with type one error (alpha) of 0.05 and beta set at 0.2 in which 60 children per group were assessed. Growth parameters (weight, height and head circumference) of 5-year-old children were evaluated. The children in both case and control groups based on the route of pregnancy were enrolled for the entire course of study.

The case group consisted of term (gestational age = 37 to 42 weeks), singleton babies whom were products of ART in Research and Clinical Center for Infertility of Shahid Sadoughi University of Medical Sciences, Yazd, Iran in 2005 and were chosen by a computer generated random number list .

The control group consisted of term, first child, singleton and spontaneously conceived 5-year-old children whom were referred for vaccination in the primary health care center of Shahid Akbari in 2010 which was also the region which the ART babies were from . Case and control matched for year of birth, area of residence, parity, gestational age, maternal weight, maternal age and socioeconomic status. Neonatal medical records of case and control groups were reviewed and variables such sex, gestational age, birth weight, length, and head circumference, route of delivery, maternal age and parity were recorded.

Multiple pregnancies, severe asphyxia, neonatal intensive care unit (NICU) admission, children with major congenital malformations, chromosomal abnormalities and genetic syndromes were excluded.

The weights of all babies were taken with a children's weighing scale with sensitivity of 10 g. The weighing scale was calibrated at regular intervals. Head circumference was measured using a flexible non-stretchable tape measure which runs from the supraorbital ridge to the occiput in the path as the maximum occipitofrontal circumference. The standing crown heel height was measured using a stadiometer. To obviate error due to interobserver variations, all measurements were made by a trained general physician of research who was not blinded to the status of the baby in the pediatric clinic of Shahid Sadoughi Hospital.

For assessment of growth parameters, National Health and Nutrition Examination Survey III (NHANES III) curves were used and body mass index (BMI) was calculated using the formula, weight in kilogram / height in metre^2. Those who were more than 95 percentile and less than 5 percentile of age and sex were considered obese and underweight respectively.[9]

Height of less than 2 standard deviation from height age was considered short stature.

Other variables such as growth parameters (weight in kilogrammes, height and head circumference in centimetres) at the 5 years of age, paternal age and maternal educational level were also reviewed.

The data were analysed using SPSS (Statistical Packages for Social Sciences) version 15 statistical software. Chi-square test or Fisher exact test were used for data analysis of qualitative variables and mean of continuous variables were compared using independent T-test and ANOVA (analysis of variance). Differences were considered significant at *P* values of less than 0.05.

This study has been approved by the ethic committee of Shahid Sadoughi University of Medical Sciences, Yazd, Iran.

Results

One hundred and twenty-two children, including 58 girls (47.5%) and 64 boys (52.5%) "with equal numbers in each group" were evaluated. Comparison of the mean maternal and paternal age between the 2 groups is shown in Table 1. No statistically significant difference was seen in both groups.

Table 2 shows the comparison of some characteristics of children in both groups, which indicates that sex distribution was similar in both groups, highly educated mothers had a higher tendency of spontaneously conceived births and their babies had a tendency of low birth weight (LBW) or birth weight less than 2500 g) and caesarean section were higher in babies born through ART.

Table 1. Comparison of Ages of Mothers and Fathers of Children in the 2 Groups

Group / Age (Years)	ART Mean ± SD	Natural conception Mean ± SD	*P* value
Mother	28.48 ± 4.22	27.1 ± 4.21	0.69
Father	35.48 ± 5.11	34.52 ± 5.03	0.3

Table 2. Comparison of Some Characteristics of Children in the 2 Groups

Data	Group	ART		Spontaneous conception		*P* value
		Number	Percentage	Number	Percentage	
Sex	Female	27	44	31	51	0.47
	Male	34	56	30	49	
Mother education level	< high school	13	21.3	5	8.2	0.04
	≥ high school	48	78.7	56	91.8	
Route of delivery	Vaginal	0	0	47	77	0.0001
	Caesarean section	61	100	14	23	
Low birth weight (<2500 g)	Yes	15	24.6	5	8.2	0.02
	No	46	75.4	56	91.8	

Table 3. Comparison of Mean of Weight, Height and Head Circumference at Birth in Both Groups

Data	ART Mean ± SD		Natural conception Mean ± SD	*P* value
	IVF	ICSI		
Weight in kilogrammes	2.84 ± 0.61	2.76 ± 0.53	3.25 ± 0.41	0.0001
Height in centimetres	48.11 ± 2.4	48.01 ± 2.2	49.61 ± 6.2	0.1
Head circumference in centimetres	33.4 ± 1.7	33.4 ± 1.3	34.62 ± 1.3	0.001

IVF: In vitro fertilisation; ICSI: Intracytoplasmic sperm injection

Table 4. Comparison of Mean of Weight, Height and Head Circumference at the Age of Five in the 2 Groups

Data	ART Mean ± SD		Spontaneous conception Mean ± SD	*P* value
	IVF	ICSI		
Weight in kilogrammes	16.5 ± 1.8	15.2 ± 2.1	17.8 ± 2.9	0.0001
Height in centimetres	105.9 ± 5.9	103.9 ± 7.4	106.5 ± 4.6	0.12
Head circumference in centimetres	51.1 ± 1.2	50.4 ± 1.9	50.5 ± 1.7	0.16

IVF: In vitro fertilisation; ICSI: Intracytoplasmic sperm injection

Comparison of mean weight, height and head circumference at birth is presented in Table 3, which indicates that ART born children had lower weight and smaller head circumference at birth.

Comparison of mean weight, height and head circumference at the age of 5 is presented in Table 4 which indicates that ART born children had lower weight.

Comparison of frequency of being underweight, obesity and having short stature in both groups is shown in Table 5, which is indicative of a higher frequency of being underweight and having short stature at 5 years of age in babies born through ART.

Discussion

Based on the results of this study, ART born children had lower birth weight, smaller birth head circumference and lower weight at 5 years of age. The frequency of low birth weight, being underweight and having short stature at 5 years of age was higher in ART children.

In this study, the mean maternal age was similar in ART and natural conception groups. There were more highly educated mothers in the natural conception group. In a study in Denmark, mothers of IVF children were older and had higher education[10] and in a study in Belgium, mothers in ICSI group were older but the educational levels of both parents was similar in the 2 groups.[11] A possible explanation could be that couples married at a younger age in southern provinces of Iran and that many of the couples who had difficulty in conceiving were referred to the infertility clinics in Yazd. On the other hand, with increased in educational levels and better knowledge of methods of diagnosis and treatment of infertility, couples tend to seek treatment earlier.

This study revealed that the rate of caesarean section was higher in assisted conception, which is in agreement to other studies.[12-15] Since ART pregnancies had a higher incidence of obstetric complications (abortion risk, placental complications, hypertension, gestational diabetes, maternal haemorrhage),[14] these pregnancies are often a source of anxiety which resulted in a significant increase in the rate of caesarean birth.[12]

This study also revealed that the mean weight at birth was lower in ART babies which is comparable to other studies.[13] Also, the frequency of LBW was higher in babies born through ART which was in agreement to other studies.[16,17]

ART babies in this study were lighter at 5 years of age. Likewise, in Koivurova et al,[18] singleton IVF children were lighter than those born of natural conception for up

Table 5. Comparison of Frequency of Being Underweight, Obesity and Short Stature in Both Groups

Data	Group	ART		Natural conception		*P* value
		Number	Percentage	Number	Percentage	
Underweight	Yes	28	45.9	11	18	0.001
	No	33	54.1	50	82	
Obesity	Yes	1	1.6	2	3.3	0.8
	No	60	98.4	59	96.7	
Short stature	Yes	18	29.5	8	13	0.02
	No	43	70.5	53	87	

to 3 years of age.

However in other studies, the weight, height and head circumference were similar in ART and spontaneous conception born children.[19-23]

On the other hand, in a study by Makhoul et al,[24] children born via IVR with very low birth weight (birth weight <1500 g) tend to be taller than those who were born via natural conception at 6 to10 years of age.

Possible explanation for these could be the differences in race, design of study, birth growth parameters, maternal health condition, gestational age, age of evaluation of children, single or multi fetal births, parental anthropometry, duration of follow-up and selection method of sample.

The LBW rate in spontaneous conception in this study was 8.2%, similar to another study conducted in Yazd by Golestan et al[25] whose LBW rate was 8.4%.[25]

The mean birth weight of term, singleton babies of spontaneous conception in this study was 3250 g. In another Iranian study,[26] the mean birth weight of neonates with mothers having a normal range of total pregnancy weight gain, was 3320 g, comparable to the other study in Tehran-Iran which found that the mean of birth weight of term singleton neonates was (3123.75 ± 492.04) g.[27]

Conclusion

The growth of a child is a dynamic process, and regular assessment of growth parameters and evaluation in periods of catch up growth is necessary for detection of growth abnormalities. Therefore, for ART babies, accurate recording of growth parameters by personnel of health centers and physicians during follow-up, and parental education about the growth process should be emphasised for early and timely diagnosis and management of growth disorders.

It seems necessary to conduct further cohort researches with larger sample size, and longer period of follow-up and with similar variables like mothers' education level and BMI, and also same reproductive conditions of parents to evaluate growth process and other outcomes in ART children in viewing their development from puberty to early adulthood.

Acknowledgments

We thank the Deputy for research of Shahid Sadoughi University of Medical Sciences, Yazd, Iran for supporting this study. We also thank staff of Research and Clinical Center for Infertility of Shahid Sadoughi University of Medical Sciences, Yazd, Iran for collating the data.

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