Original Article

Iran J Pediatr
Dec 2011; Vol 21 (No 4), Pp: 449-454

Evaluation of the Growth Process of Infants Conceived by Assisted Reproductive Techniques at Royan Institute from Birth to 9 Months

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Received: *May 21, 2010*; Final Revision: *Dec 18, 2010*; Accepted: *Mar 15, 2011*

Abstract

Objective: Due to recent scientific progress in assisted reproductive techniques (ART), infertile couples can now become fertile. Thus, a number of infants in our country are the results of these costly interventions. This study has been undertaken to evaluate the physical growth process of different methods of ART infants by standard growth charts from birth until nine months of age.

Methods: This was a descriptive cross-sectional study of 333 infants conceived through ART [intracytoplasmic sperm injection (ICSI) and *in vitro* fertilization (IVF)] at Royan Institute. A sequential, non-random sampling method in a period of 22 months was used. Their growth was assessed by measuring infants' weight, height and head circumference, and physical examination. The growth patterns were calculated by recording the values in standard growth charts. The final analysis was done with SPSS version 16 and by using Chi-square test.

Findings: In comparison with growth charts, the weights of one-third of the infants were less than two standard deviations (SD) at birth and one-fourth had head circumference less than three SD at birth. Low birth weight (LBW) infants were six times more than infants of normal population. From birth to six months of age, growth abnormalities were seen in a substantial number of infants. However, at nine months of age, there was no significant difference observed between infants conceived by different methods of ART (IVF and ICSI).

Conclusion: Multiple births are the most important confounding factor impacting the growth process of ART infants. Multiple pregnancies can lead to low birth weight, height and head circumference, and growth abnormalities up to six months of age. This abnormality improves by increasing age of the infants.

Iranian Journal of Pediatrics, Volume 21(Number 4), December 2011, Pages: 449-454

Key Words: Assisted reproductive techniques; Low birth weight; Growth index; *in vitro* fertilization; intracytoplasmic sperm injection

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Introduction

Approximately one million children are born worldwide through assisted reproductive techniques (ART)[1]. In many developed countries, ART conceived children constitute 2-4% of all born children[2]. The most important problems of ART are the result of prematurity and low birth weight (LBW)[3,4]. In three studies, prematurity and LBW in ART children was 4-5 times more than in normal population[5-7].

In five other case-control studies on ART children, the rate of prematurity and LBW was almost two times more than that seen among single, normal conceived children[8-12].

Prematurity and LBW increase the probability of neonatal death, neonatal complications, congenital malformations and diseases[13,14]. The most important factors which cause prematurity and LBW in these infants are multiple pregnancies and transferring of more than one embryo. Decreasing numbers of transferred embryos from three to two, reduce 70% IVF induced preterm births by reducing multiple pregnancies[7]. For unknown reason, in singleton transferred embryo, both LBW and prematurity still occur with a greater frequency among ART conceived children in comparison to single normal conceived children[14,15].

A few studies have been done on the growth process of these children, however the problem with follow-up and parental belief about a lack of growth difference between their children and other normal conceived children are causes of limitation of sampling in these studies.

In one study that compared 299 *in vitro* fertilized (IVF) children with 588 normal conceived ones, the IVF children had a lower weight and height at birth than the control group. At one year of age the growth rate increased, however they ultimately had a lower weight at three years of age than the control group, with no reported difference in height[16].

In six studies, there were no significant difference in height, weight and head circumference between infants who were conceived by ART and the control group[1,17-21].

Regarding the importance of this subject and the lack of a comprehensive study on the physical growth process of ART infants in Iran, this study was designed to compare the growth process of children conceived with different methods of ART (IVF and ICSI) by standard growth charts from birth until nine months of age.

Subjects and Methods

This was a descriptive, analytic, cross sectional study approved by the Research Ethics Committee of the Academic Center of Education, Culture and Research (ACECR) and Royan Institute. During a 22 month period, a pediatrician performed two examinations (first time between birth to 6 months and second time between 6-9 months) on 333 ART children that were conceived by IVF and ICSI methods in Royan Institute with the parents' written consent. The sampling method was non random, sequential with the inclusion criteria of infants conceived through one kind of ART methods (IVF, ICSI) and birth date from September 2007 to July 2009 and residence in Tehran. If infants did not come for the second examination, they were excluded from study. Information was gathered through interviews, clinical examinations and medical records. Information on the infants' weight, height, and head circumference at birth were obtained from birth chart and interviews with their mothers. A pediatrician checked the infants' height (with measure mat in supine position), weight (with Seca digital scale) and head circumference (with tape) at each visit. The results were recorded in the infants' medical records and on standard growth charts. The patterns of weight gain and increasing of height (greater or less than 2SD) and pattern of increasing of head circumference (greater or less than 3SD) were obtained. Analysis was done with SPSS version 16 and Chi-square test. P-value <0.05 was considered statistically significant.

Findings

There were 333 infants evaluated two times in this study, 173 (52%) were male and 160 (48%) female. There was a total of 108 (32%) LBW

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Table 1: Distribution of growth factors at birth in children born by ART

Parameter		IVF Number (%)	ICSI Number (%)	ART Number (%)	*P*-value
Number of neonates		54 (16.2)	279 (83.8)	333 (100)	
Weight	**<2500g**	13 (24)	95 (34)	108 (32)	0.15
	2500-4000g	41 (76)	184 (66)	225 (68)	
Height	**<45cm**	6 (11)	58 (20.7)	64 (19.2)	0.07
	45-55 cm	48 (89)	221 (79.3	269 (80.8)	
Head circumference	**<33 cm**	10 (18.5)	82 (29.3)	92 (27.6)	0.2
	33-37 cm	43 (80)	190 (68.2)	233 (70)	
	> 37cm	1 (1.5)	7 (2.5)	8 (2.4)	

IVF: *in vitro* fertilization; ICSI: intracytoplasmic sperm injection

neonates in this study, of which 24 (7%) were single deliveries and 84 (25%) multiple deliveries.

Of all LBW neonates, 13 (3.9%) were IVF LBW neonates, of which 4 (1.2%) were the result of single pregnancies and 9 (2.7%) of multiple pregnancies.

From 95 (28.5%) ICSI LBW neonates, 17 (5.1%) resulted from single pregnancies and 78 (23.4%) from multiple pregnancies (Table 1).

Table 2 shows the distribution of weight, height, and head circumference in the two times of assessment (birth to 6 months and 6-9 months of age) in children born by ART.

Discussion

The most important problem in evaluating ART children is lack of comparability with normally conceived children, which is due to several factors: background disorders of parental infertility, different drugs used in assisted reproductive technique process and for fetal survival, increased emotional stress in these parents and more exposure to environmental factors. Clearly the best study group are those children who have been spontaneously born to infertile parents without treatment or with use of non-invasive

Table 2: Distribution of growth factors in children born by ART

Parameter		IVF Number (%)	ICSI Number (%)	ART Number (%)	P value
Weight gain (Birth to 6 months)	**> 2 SD decrease**	1 (1.8)	13 (4.5)	14 (4.2)	0.08
	Appropriate	47 (87)	203 (73)	250 (75)	
	>2 SD increase	6 (11)	63 (22.5)	69 (20)	
Weight gain (6-9 months)	**> 2 SD decrease**	1 (1.8)	12 (4.3)	13 (3.9)	0.6
	Appropriate	45 (83.4)	235 (84.5)	280 (84)	
	> 2 SD increase	8 (14.8)	32 (11.4)	40 (12.1)	
Height increase (Birth to 6 months)	**> 2 SD increase**	1 (1.8)	28 (10)	29 (8.7)	0.001
	Appropriate	53 (98.2)	251 (90)	304 (91.3)	
Height increase (6-9 months)	**>2 SD increase**	0	8 (2.8)	8 (2.4)	0.4
	Appropriate	54 (100)	271 (97.2)	325 (97.6)	
Head circumference increase (Birth to 6 months)	**<3 SD curve**	1 (1.8)	6 (2.1)	7 (2.1)	0.9
	Appropriate	51 (94.5)	266 (95.3)	317 (95.2)	
	>3 SD curve	2 (3.7)	7 (2.5)	9 (2.7)	
Head circumference increase (6-9 months)	**<3 SD curve**	1 (1.8)	5 (1.8)	7 (2.1)	0.8
	Appropriate	52 (96.4)	264 (94.7)	315 (94.6)	
	>3 SD curve	1 (1.8)	10 (3.5)	11 (3.3)	
Total		54 (16.2)	279 (83.8)	333 (100)	

IVF: *in vitro* fertilization; ICSI: intracytoplasmic sperm injection
Appropriate=50% weight of infants in that age according to NCHS/WHO standard chart.
(<2SD) or (>2SD)=2SD less or more than 50% weight of children in that age according to NCHS/WHO Standard chart.

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methods other than IVF or ICSI (like ovulation induction), which is not practical. On the other hand, there are published articles that compare ART children with normal conceived children or children conceived with the use of different methods of assisted reproductive techniques.

In this study 32% of the children were LBW which is approximately six times greater than LBW infants in general population (5.33%) who have been born in Tehran[22]. Of these, ICSI infants have the highest (34%) frequency. In three studies which have reported the rate of LBW in ART children, the results have shown a 4-5 times higher rate than in the normal population[5-7]. In six studies, however, this rate was two times higher than normal conceived children[8-12,15]. 7% of LBW newborns were single deliveries which are higher than LBW newborns of normal conception in Tehran [22].

The rate of LBW infants in the ICSI and IVF groups were similar and there was no significant difference between the two groups (*P*=0.152). The LBW risk ratio (RR) in ICSI infants, when compared with the IVF group, was 1.4, which was different from that (1.03) in other studies [23].

In some studies there was no significant difference in birth weight between the ICSI and IVF groups [24-26]. Two of the most common reasons for LBW in these children are multiplicity and infertility background disorder.

In one study which compared neonatal birth weight of IVF and ICSI infants with infants of previously infertile women achieving pregnancy after sexual intercourse, neonatal birth weight is significantly lower in infants born after IVF and ICSI methods than those in the other group and they concluded that ART has specific effect on lowering of neonatal birth weight [27].

In this study, both height and head circumference of ART children were respectively 19.2% and 27.6% at birth less than general population infants according to standard growth curves [22].

A reason could be that multiplicity was higher in the ART group when compared with general population (25% vs 0.3% respectively)[22]. In one study which compared IVF children with normally conceived children, there was a noticeable difference in height at birth[17].

In this study, the pattern of weight gain from birth to 6 months and 6-9 months, according to standard growth curves, showed that 4.2% and 3.9% of these children had more than 2SD decrease in weight gain respectively. This pattern gradually improved, by six months and thereafter.

Infants showed an appropriate weight gain (75% and 84%, respectively). Weight gain disorder was lower in IVF infants and there was no significant difference in weight gain of IVF and ICSI group. The rate of infants with a weight gain of greater than 2SD from birth to 6 months and 6-9 months were respectively 20% and 12.1%, which reached the level of general population of infants with increasing of age. In one study ART infants had a faster growth and evidence of catch up in both height and head circumference from 6 months to 18 months old compared with infants born with natural conception [28].

Of these infants, 8.7% had a height increase disorder of more than 2SD until 6 months. A gradual improvement was noted until 9 months, while only 2.4 % of infants showed a height increase disorder of greater than 2SD. Of the two groups, the ICSI infants showed more delay in height increase until the age of 6 months.

Increase of head circumference was appropriate for age in 95.2% of these children until 6 months of age and in 94.6% until 9 months of age. This process is the same in both groups and there is no significant difference between the two groups.

In one study, IVF infants at birth were compared with the normal population for weight, height and head circumference. The IVF newborns had lower birth weights and heights and head circumference, at 1 year of age they had an increase in growth however, at 3 years of age they had a lower weight when compared with the control group but the height and head circumference were similar[16]. However, six studies have shown no significant differences in height, weight, head circumference and physical growth between ART children and normal conceived children [1,17-21]. In a recent study in UK which follows these children in various time points, no significant differences were observed regarding head circumference, height and weight between ICSI and IVF groups [29].

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Limited sample size, difficult access to this group of infants and their families and الغفكقفف ذكمه of parents for re-examination of infants cause the results less reliable. In the future, selecting a greater number of newborns and implementing them in prospective studies with longer duration should be considered for better and more reliable results.

Conclusion

The most important confounding factor which affects the growth status of ART infants is multiplicity which can lead to low birth weight, height and head circumference at birth. Although the higher number of ART infants showed diminished growth patterns of weight, height and head circumference from birth until 6 months according to standard charts, but growth indexes improved until 9 months and there was no significant difference in the growth process between IVF and ICSI infants.

Acknowledgment

The authors express their gratitude to the Academic Center for Education, Culture and Research (ACECR) for its financial support and to Mrs Khademi and Miss Dadashloo for their cooperation. There is no conflict of interest in this study.

Conflict of Interest: None

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