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Original Article (Pages: 14726-14736)

Comparison of the Developmental Status in Children Born Following Assisted Reproductive Technology and Spontaneous Pregnancy

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Abstract

Background: The assisted reproductive technology (ART) is an important option for fertility in infertile couples. The aim of infertility treatment is not only pregnancy, but also healthy children. However, there are challenges to the development of children born following ART. The present study aimed to compare the developmental status of children born following ART and spontaneous pregnancy.

Methods: The study was a retrospective cohort study that investigated 84 children born following ART and 168 children born following spontaneous pregnancy at the same age. They had referred to comprehensive health centers of Isfahan in 2019.

The cases were selected through systematic random sampling. Data collection tools included the researcher-made demographic information questionnaire, and the standard Ages and Stages Questionnaire (ASQ). We evaluated the children's development in five developmental domains, namely communication, gross motor, fine motor, problem-solving, and personal-social domains. The data was analyzed using descriptive and analytical statistics in SPSS version 21 at a significance level of <0.05.

Results: Analysis of covariance after adjusting the demographic variables indicated that the developmental domains were not significantly different in children born following ART and spontaneous pregnancy (P>0.05). Pearson correlation coefficient test showed gross motor had a statistically significant association with the child's age (p =0.24, r = 0.075), birth weight (p =0.47, r = 0.045), current weight (p =0.34, r = 0.061), and current height (p =0.30, r = 0.066).

Conclusion: There was no statistically significant difference in the development of children born following ART and Spontaneous pregnancy. The gross motor had a statistically significant association with some demographic information of children.

Key Words: Assisted reproductive technology; Child; Development; Spontaneous pregnancy.

*Please cite this article as: Roosta L, Savabi-Esfahani M, Nasr-Esfahani M, Torabi F Comparison of the Developmental Status in Children Born Following Assisted Reproductive Technology and Spontaneous Pregnancy. Int J Pediatr 2021; 9 (11):14726-14736. DOI: **10.22038/IJP.2020.53611.4250**

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Received date: Nov.17,2020; Accepted date:Dec.01,2020

1- INTRODUCTION

Infertility in a couple's life can affect different aspects of their life (1). This problem refers to the lack of pregnancy after a year of sexual intercourse without using contraceptive methods (2). Infertility is a common problem worldwide. The prevalence of infertility is 8-12% in the world, and about 21-22% in Iran (3, 4). The ART is an important option for couples with infertility to have pregnancy (5). Almost 56% of infertile couples use medical treatments and ART that covers approximately 2% of live births (2, 6). Increasing the success of ART and the couples' knowledge and insight has led to the increasing use of ART (7). The purpose of ART is not only the birth of a child, but also the infant's health (8). There are challenges to the adverse consequences of these methods in children; hence, the knowledge about the adverse consequences in these children is very important (9, 10).

Children are the future makers and the most important capital of any country (11) and their upbringing is a main goal of social and economic development programs. Therefore, the spiritual, social, physical, and mental health should be taken into consideration to achieve these goals (12). Furthermore, attention to children's health has always been emphasized as a vulnerable group (13).

Evaluation of development is of great importance as an important domain of child health (14). The child's development is a gradual process that begins before birth and continues throughout life, but the age before 5 is the fastest period of growth and development of a child (15, 16).

Children's development is classified into the motor, communication, problem-solving, and personal-social domains (13). Several factors, including biological, psycho-social, and inheritance factors affect children's development (15, 17).

Some studies have found that ART may affect the health of these children and be associated with higher risks of learning disabilities in them (18). However, Aoki et al. found that children born following ART had higher linguistic development than children born following normal fertility at the age of 36 months (19). Another study, likewise, indicated that ART was not associated with the risk of developmental delay (20).

Investigating the status of child development for the early diagnosis of developmental disorders is an essential part of basic health measures (21). Furthermore, these studies can lead to early interventions in children with developmental delays (22).

Despite the challenges to the developmental status of children born following the ART, there are few studies in Iran on the developmental status of children born following ART. Therefore, the present study aimed to compare the developmental status in children born following ART and spontaneous pregnancy.

2- Materials and Methods

2.1- Study Design and Population

The study was a retrospective cohort study. The sample size was determined based on the below formula with a 95% confidence interval, 80% power and d equal to 0.43s.

$N = (Z1 + Z2)^2 (2 S^2) / d^2$. The samples thus consisted of 84 children born following ART and 168 children born after spontaneous pregnancy. They had referred to comprehensive health centers of Isfahan in 2019.

2-2. Methods

We first prepared a list of mothers who lived in Isfahan and used the ART in the last 5 years at a Fertility and Infertility Center, Isfahan, Iran. After obtaining their

informed consent, they were invited to participate in the study. The researcher went to the 52 comprehensive health service centers of Isfahan where the children had received their care.

For each child born following the ART, we selected two children from spontaneous pregnancy at the same age from the same comprehensive health service center and assessed their development. The 168 children born after spontaneous pregnancy in 52 comprehensive health service centers were selected through systematic random sampling.

The demographic information was collected using the registration systems of the comprehensive health centers.

2-3. Measuring tools: validity and reliability

Data collection tools included a demographic researcher-made questionnaire in order to obtain demographic information of mothers and children, and the Ages and Stages Questionnaire (ASQ).

The demographic questionnaire contained the child's age and gender, birth and current weight, height and around the head, birth rank, as well as the number of children, birth status (term and preterm), mother and Father's age, mother and Father's job, mother and Father's education, monthly household income, number of maternal pregnancies and deliveries, number of family members, and the delivery method.

The questionnaire was developed in the 1970s by Dr. Breaker at the University of Oregon in the United States to design a low-cost, valid, and culturally sensitive screening system for child development. Workie et al. reported the validity and reliability of ASQ as 0.83-0.88 and 0.90-0.94, respectively (23). Also Vameghi et al. showed that the validity of the Persian version of ASQ was satisfactory. They reported the reliability of ASQ as 0.76 - 0.86 (24).

The questionnaire consisted of 19 scales for examining the development of children aged 4 to 60 months. The parents responded to the questionnaires. Each scale contained 30 questions that were classified into 5 domains, namely communication, gross motor, fine motor, problem-solving, and personal-social domains. There were six questions for each domain of development in each age group (25). They included questions such as does the child walk well? And does the child draw a line with the tip of a pencil? Each question has three answers: yes, sometimes and no. The scoring is defined by giving 10 to the answer yes, 5 to sometimes, and zero to not yet. The minimum and maximum points were zero and 60 in each domain, respectively. The final score of each domain is compared with the cut-off points of the ASQ guidelines after summation (20).

2.4-Ethical consideration

This study was approved by the Ethics Committee of Isfahan University of Medical Sciences with a number of IR.MUI.RESEARCH.REC.1398.185.
Participation in the study was anonymous and with informed consent.

2-5. Inclusion and exclusion criteria

In the study, Inclusion criteria were no physical abnormality, singleton or twin children, living with both parents, and a child between 4 and 60 months of age.

2-6. Data Analyses

The data were analyzed by SPSS version 21 with a significance level of less than 0.05.

We used the independent t-test, Fisher's, Mann-Whitney, and Chi-square tests to investigate the differences in demographic variables between the two groups (children from ART and spontaneous reproduction).

We assessed the scores of the developmental domains (communication, problem-solving, gross motor, fine motor, and personal-social movements) using descriptive tests (mean and standard deviation). The analysis of covariance was used after adjusting the demographic variables to compare domains of development in the two groups. Then, we utilized the logistic regression test to investigate the relationships between demographic characteristics and domains of development. The Kolmogorov-Smirnov test was used to check normal distribution.

3- Results

In the present study, we studied 252 children among whom 168 children (66.7%) were born by spontaneous pregnancy and 84 children (33.3%) were born using ART. Comparison of the children's gender, birth condition, mother and father's job, delivery method, mother and Father's education, as well as the number of children, monthly household income, and birth rank have been shown in **Table 1**. The mean ages of the mothers in spontaneous pregnancy and ART were, respectively, 31.83±5.15 and 34.94±4.69 at the time of the study; and 30.05±5.14 and 33.11±4.9 years at the time of the child's birth. The mean ages of the fathers of the children from spontaneous pregnancy and ART during the study were 39.14±5.43 and 36.36±5.44, and at the time of the child's birth 37.35±5.61 and 34.62±5.47 years, respectively. The results indicated that the mean age of fathers and mothers at birth and during the research were higher in the ART group than the spontaneous pregnancy group (P<0.001). Results of Fisher's and Mann-Whitney tests indicated that the frequency distribution of maternal gestational age at birth, parents' jobs, child sex, number of infants, parents' education level, and monthly income level were not significantly different between the two groups. However, the frequency distribution of cesarean delivery in the ART group was significantly higher than that in the spontaneous pregnancy group.

There was a statistically significant difference between the birth orders in both groups (P<0.001) (**Table 1**).

Table 2 shows the comparison between the mean scores of the developmental domains in children by some demographic information of children in the two groups. As shown in **Table 2** there was no statistically significant difference between mean scores of developmental domains in girls and boys, cesarean section and vaginal delivery method, number of singleton and twins (P>0.05).

The test also indicated that the mean scores of communication were significantly lower in preterm children than in other children (P<0.05). However, the mean of other domains of development were similar between term and preterm children (P>0.05) (**Table 2**).

Comparison of Domains of development in the two groups has been shown in **Table 3**, which indicates the mean scores of communication, gross motor, fine motor, problem-solving, and personal-social.

The normal range of domains of development scores were from 0 to 60. Mean scores of communication, gross motor, fine motor, problem-solving, and personal-social zones were 56.7 ±5.1, 53.72 ±6.94, 54.88 ±4.83, 55.09 ±5.15, and 55.39 ±5.36 in the group of children with spontaneous pregnancy, and 56.13 ±5.11, 54.82 ±6.79, 54.94 ±5.57, 55.12 ±4.78, and 55.18 ±5.4 in children born following ART.

Covariance test did not show any statistically significant difference between developmental domains in two groups after adjusting for demographic variables (paternal and maternal age at birth and during the study) (P>0.05) (**Table 3**).

Table-1: Comparison of Demographic and fertility information in the two groups

Groups	Spontaneous pregnancy		ART			
Variables	No	Percent	No	Percent	χ^2	p
Child gender						
Boy	78	46.4	42	50	0.29	0.59
Girl	90	53.6	42	50		
Birth condition						
Preterm	9	5.4	5	6	-	0.53
Term	159	94.6	79	94		
Father's job						
Unemployed	3	1.8	1	1.2	5.8	0.21
Manual worker	14	8.3	13	15.5		
Employee	52	31	21	25		
Self-employment	99	9.58	49	58.3		
Mother's job						
Housekeeper	148	88.1	77	91.7	0.75	0.39
Employee	20	11.9	7	8.3		
Cesarean section	92	54.8	84	100	54.41	<0.001
NVD*	76	45.2	0	0		
Number of children						
Single	164	97.6	82	97.6	-	1
Twin	4	2.4	2	2.4		
Mother's education						
Elementary	20	11.9	15	17.9	0.16	0.87
High school	58	34.5	22	26.1		
University	90	53.6	47	56		
Father's education						
Elementary	35	20.8	18	21.4	0.45	0.65
High school	56	33.3	30	35.7		
University	77	45.9	36	42.9		
Monthly household income (Rials)						
Under 10 million	9	5.4	7	8.3	1.76	0.08
10-20 million	56	33.3	36	42.9		
20-30 million	58	34.5	23	27.4		
Over 30 million	45	26.8	18	24.4		
Birth rank						
One	96	57.1	79	94	5.91	<0.001
Two	61	36.3	4	4.8		
three	11	6.5	1	1.2		

* Normal vaginal delivery

Table-2: Comparison of the mean scores of developmental domains in children by birth status, delivery method, child gender and number of children

Variables		Birth status		t	p
Domains		Preterm	Term		
	Communication	53.21±6.68	56.7±4.94	2.51	0.01
	Gross motor	51.43±10.64	54.24±6.61	1.49	0.14
	Fine motor	55.36±4.99	54.87±5.09	0.34	0.73
	Problem solving	55.71±4.32	55.06±5.06	0.47	0.64
	personal-social	53.93±5.61	55.4±5.35	0.99	0.32
Variables		Delivery method			
Domains		SC	NVD		
	Communication	56.25±5.36	57.11±4.42	1.22	0.22
	Gross motor	54.18±6.57	53.88±7.64	0.31	0.76
	Fine motor	54.86±5.36	55±4.32	0.22	0.82
	Problem solving	55.03±5.03	55.26±5.03	0.34	0.73
	personal-social	55.31±5.16	55.33±5.85	0.02	0.98
Variables		Child gender			
Domains		Boy	Girl		
	Communication	56.58±4.89	56.44±5.3	0.22	0.82
	Gross motor	54.46±5.79	53.75±7.77	0.81	0.42
	Fine motor	54.46±5.1	55.3±5.05	1.32	0.19
	Problem solving	55.42±4.96	54.81±5.07	0.96	0.34
	personal-social	54.71±5.47	55.87±5.22	1.72	0.09
Variables		Number of children			
Domains		Single	Twin		
	Communication	56.65±5.01	50.83±5.84	2.41	0.06
	Gross motor	54.21±6.6	50.17±14.97	0.82	0.45
	Fine motor	54.86±5.1	56.67±4.08	0.86	0.39
	Problem solving	55.1±5.04	55±4.47	0.05	0.96
	personal-social	55.32±5.39	55±4.47	0.15	0.88

The relationships between some demographic characteristics in children with domains of development are shown in **Table 4**. The result of Pearson correlation showed that gross motor had a statistically significant association with the child's age (p=0.24, r= 0.075), birth weight (p=0.47, r=0.045), current weight (p=0.34, r=0.061), and current height (p =0.30, r = 0.066) while no significant relationship was observed with other variables including mother and father's age, number of maternal pregnancies and deliveries, number of family members, birth height and around the head, current around the head and birth rank(P>0.05). Furthermore, it did not show any statistically significant relationship between domains of communication, Fine motor, Problem solving, personal-social and parental and maternal age at childbirth (P>0.05) (**Table 4**).

4- DISCUSSION

The present study aimed to compare the developmental status in children born Following ART and spontaneous pregnancy.

Results of the study indicated that there was no statistically significant difference between different domains of development, including communication,

gross motor, fine motor, personal-social domain, and problem-solving in children born following ART and spontaneous pregnancy.

Table-3: Comparison of the Domains of development in the two groups

Groups	Spontaneous pregnancy		ART		$F_{242,1}$	P
Domains	Mean	SD	Mean	SD		
Communication	56.7	5.1	56.13	5.11	0.74	0.39
Gross motor	53.72	6.94	54.82	6.79	1.14	0.29
Fine motor	54.88	4.83	54.94	5.57	0.42	0.52
Problem solving	55.09	5.15	55.12	4.78	0.11	0.74
personal-social	55.39	5.36	55.18	5.4	0.34	0.56

Table-4: Correlation coefficients between the scores of children's developmental domains and demographic variables

Domains	Communication		Gross motor		Fine motor		Problem solving		personal-social	
Variables	r	p	R	p	r	p	r	p	r	p
Child age	0.083	0.19	0.152	0.02	0.009	0.89	0.042	0.51	0.075	0.24
Father's age	-0.102	0.11	-0.033	0.6	0.018	0.78	0.07	0.26	-0.026	0.68
Mother's age	-0.082	0.2	-0.082	0.2	-0.023	0.72	0.069	0.27	-0.025	0.69
Number of maternal pregnancies	0.007	0.91	-0.011	0.86	-0.121	0.06	0.061	0.34	0.006	0.92
Number of maternal deliveries	-0.015	0.81	-0.032	0.61	-0.124	0.49	0.028	0.65	-0.014	0.82
Number of family members	-0.049	0.44	-0.072	0.26	-.0107	0.09	0.033	0.6	-0.03	0.63
Birth weight	0.082	0.2	0.132	0.04	0.033	0.61	-0.024	0.7	0.045	0.47
Birth height	0.06	0.34	0.023	0.71	0.004	0.95	-0.026	0.68	-0.083	0.19
Birth around the head	0.05	0.43	0.122	0.054	0.005	0.94	0.013	0.83	0.07	0.27
Current weight	0.045	0.47	0.128	0.047	0.008	0.90	-0.028	0.66	0.061	0.34
Current height	0.095	0.13	0.13	0.04	-0.005	0.94	0.054	0.39	0.066	0.3
Current around the head	0.041	0.69	0.002	0.98	-0.092	0.38	-0.055	0.6	-0.087	0.41
Birth rank	-0.027	0.67	-0.031	0.62	0.121	0.06	0.007	0.91	-0.074	0.24

Results of a study by Yeung et al and Aoki et al also indicated that there was no statistically significant difference in the field of communication development between children born from ART and spontaneous pregnancy (19, 26). Researchers believe that children's communication with others may be influenced by the way the parents interact with children, parenting styles, and exposure to environmental and verbal stimuli so that these factors may lead to higher self-confidence in children and better creation of communication in them (19,31). Two other studies by Hashimato et al and Balayla et al on the development of gross motor in children resulting from spontaneous pregnancy and ART revealed that there was no statistically significant difference between these groups (27, 28). Despite the use of Ability for Basic Movement Scale for Children (ABMS-C)

and the Kinder Infant Development Scale in the Hashimato's et al. and Balayla's et al. studies and the ages and stages questionnaire (ASQ) in the present study, results of the present study were similar to the Hashimato's et al. and Balayla's et al. studies in terms of the range of motor skills (27, 28).

In another study by Bay et al. and Lung et al., investigating the fine motor development in children born from spontaneous pregnancy and ART, no significant difference was found between the two groups (5, 18). Researchers have proposed that the proper care of children in the field of movement and the situation of the children are effective in the motor development of children. Children, who are exposed to training and experience of more motor skills, have better fine motor development (29). It appears that the lack of difference in the development of fine motor between the two groups in the present study was due to the influence of other factors that should be discussed in further studies. Balayla et al. reported that no differences were found in the cognitive development of children born following spontaneous pregnancy and ART; however, the results of a study by Fallah et al. indicated that developmental delay in problem-solving was more common in children born from ART (27, 30). In this regard, some researchers believed that the quality of children's care was directly related to their cognitive development (31). The similarity of the present study to that of Balayla et al. may be related to the quality of child care that requires further studies. The difference between the results of the present study and Fallah's et al. study might be attributed to the differences in the age groups of children and the sample sizes. Fallah et al. only investigated the development of 5-year-old children, but the present study examined the age group of 4 to 60 months. The present study considered two children born following normal fertility, while Fallah et al. evaluated each child born following ART in comparison to one child born following normal fertility. The results of Yeung's et al. research also did not report any statistically significant difference between the two groups in the personal-social domain of development (20).

Kelly Vance et al. found that mothers, who used ART, were older than those with normal fertility; and there were differences in gestational age between the two groups. The results of the present study were similar to the Kelly Vance's et al study in terms of mother's age, but inconsistent in terms of difference in gestational age (32).

Furthermore, Yeung et al. compared the singletons with twins and found that twins had a slightly higher risk in the developmental delay (26). The researchers also declared that prematurity and low birth weight were more common in twin children. These factors might, thus, affect the development of the children (33). The difference in the results of the present study with Kelly Vance's et al. study might be due to the differences in birth weight and gestational age of the children.

Various studies have been conducted worldwide on comparing the developmental status of children born following ART and spontaneous pregnancy, but only few studies have evaluated the age group of 4 to 60 months. In the present study, the ART group was similar to those from spontaneous pregnancy in terms of age. Therefore, two children in the spontaneous pregnancy group were selected in comparison to each child in the ART group and they were similar in terms of the time of birth.

Since the present study had a retrospective cohort design, few mothers reported the types of assisted reproductive technique; hence, it was impossible to compare the children's development based on different types of ART. Therefore, further

prospective cohort studies should be conducted in this field.

Findings of the present study may be useful in evaluating the developmental status of children born following ART.

5- STUDY Limitations

One of the limitations of the study can be the lack of children born with ART who died before 5 years due to developmental defects.

6- CONCLUSION

There was no statistically significant difference in the development of children born following ART and spontaneous pregnancy. For all girls and boys, cesarean section and vaginal delivery methods, singletons and twins born following ART and spontaneous conception, the results of the development showed no significant differences. The gross motor had a statistically significant association with some demographic information of children. It is thought that the findings of the present study are useful for evaluating the development of children born following ART. Moreover, considering factors related to different domains of development may help healthcare providers in counseling and conducting follow-ups for the children.

7- ACKNOWLEDGMENTS

The authors are grateful to the staff of the Fertility and Infertility Center and Comprehensive Health Service Centers as well as the participants of the study for their great cooperation in this research.

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