



## Psychiatric Evaluation of Children Born with Assisted Reproductive Technologies and Their Mothers: A Clinical Study

### Yardımcı Üreme Teknikleriyle Doğmuş Çocukların ve Annelerinin Psikiyatrik Değerlendirmesi: Klinik Bir Çalışma

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#### ABSTRACT

**Background:** The number of parents who have children through assisted reproductive technologies (ART) is increasing. In this cross-sectional study, we aimed to evaluate the psychiatric diagnostic profiles and behavioral characteristics of children born after ART as well as to evaluate the anxiety and depressive symptoms in their mothers.

**Methods:** Thirty-five children (13 girls and 22 boys) born after ART (ART group) were compared with 35 naturally conceived children, matched for gender and age (control group). The Kiddie Schedule for Affective Disorders and Schizophrenia, the Diagnostic and Statistical Manual of Mental Disorders, 4th. Edition (DSM-IV) criteria and the Child Behavior Checklist (CBCL) were used for evaluation of the children. The Beck Depression Inventory (BDI) and the State-Trait Anxiety Inventory (STAI) were used for evaluating their mothers..

**Results:** The most common psychiatric diagnoses were attention deficit hyperactivity disorder, pervasive developmental disorders and anxiety disorders in both groups. Feeding disorders were significantly more frequent in children born following ART than in controls. Mothers of ART group had higher scores in BDI and STAI. Between both groups, there was a statistically significant difference in some CBCL subscales (e.g. withdrawn, social problems, internalizing and externalizing problems).

**Conclusion:** It is important to know that children born after ART may have some behavioral and psychiatric problems and working with their mothers' psychological status is also important. (*Archives of Neuropsychiatry 2013; 50: 59-64*)

**Key words:** Assisted reproductive technologies, children, anxiety, depression

**Conflict of interest:** The authors reported no conflict of interest related to this article.

#### ÖZET

**Amaç:** Yardımcı üreme teknikleriyle (YÜT) çocuk sahibi olan annelerin sayısı artmaktadır. Bu çalışmada, YÜT ile doğmuş çocukların psikiyatrik tanı profilleri ve davranış özellikleri ile annelerinin anksiyete ve depresif belirtilerinin değerlendirilmesi amaçlanmıştır.

**Yöntem:** YÜT ile doğmuş otuz beş çocuk (13 kız, 22 erkek), cinsiyet ve yaş bakımından eşleştirilmiş 35 doğal yollarla doğan çocuk ile karşılaştırılmıştır. Çocukların değerlendirmeleri için Okul çocukları için Affektif Bozukluklar ve Şizofreni Görüşme Çizelgesi, DSM IV tanı kriterleri, Çocuklar için Davranış Değerlendirme Ölçeği (ÇDDÖ) kullanılmıştır. Beck Depresyon Envanteri (BDE) ve Süreklilik ve Durumluluk Kaygı Envanteri (SDKE) annelerin değerlendirmelerinde kullanılmıştır.

**Bulgular:** Her iki grupta da en sık görülen psikiyatrik tanımlar, dikkat eksikliği hiperaktivite bozukluğu, yaygın gelişimsel bozukluklar ve anksiyete bozuklukları idi. YÜT ile doğmuş çocuklarda, kontrol grubuna göre anlamlı olarak daha fazla yeme ve beslenme bozukluğu tanısı bulunmaktaydı. YÜT grubunun annelerinde BDE ve SDKE puanları daha yüksek olarak bulundu. Her iki grup arasında bazı ÇDDÖ alt ölçeklerinde (içe çekilme, sosyal sorunlar, içe atım ve dışa atım sorunları) istatistiksel olarak anlamlı farklılık bulunmuştur.

**Sonuç:** Bu grup çocukların bazı davranışsal ve psikiyatrik sorunlarının olabileceğini bilmek ve annelerin psikolojik durumlarıyla çalışabilmek önemlidir. (*Nöropsikiyatri Arşivi 2013; 50: 59-64*)

**Anahtar kelimeler:** Yardımcı üreme teknikleri, çocuklar, anksiyete, depresyon

**Çıkar çatışması:** Yazarlar bu makale ile ilgili olarak herhangi bir çıkar çatışması bildirmemişlerdir.

#### Introduction

Since the assisted reproductive technologies (ART) developed in recent years, the number of people using these methods has increased. Emotional distress can be a cause or a result of infertility. Previous studies reported that emotional distress is associated with lower pregnancy rates, and also long-awaited

pregnancies are emotionally vulnerable and women, who are receiving treatment for infertility, have high anxiety levels. Likewise, duration of infertility, history of unsuccessful in vitro fertilization treatment and some other factors in this period have a negative impact on psychological health status and marital quality (1). Individuals, who tried several techniques for having a child and had losses (abortion), may have difficulties in the mourning process of

previous losses and high level of anxiety as well as fear of loss of their new newborns (2,3,4,5). The depression of the mother can affect the relationship between the mother and the child and can also have negative effects on the cognitive development of the child (6). Naturally conceived children with feeding problems may have mothers with history of a pregnancy losses and unsolved mourning processes (7). Babies born after ART are special children for the parents and they have to repair the psychological status of the parents, who had many losses and unsuccessful pregnancy trials, and to replace the previous losses.

Another important issue in ART is the high rates of multiple births. Mothers having twins or triplets after ART, report more negative emotions like tiredness, unhappiness and distress than the mothers of singletons (5,8). Women who were pregnant after in vitro fertilization (IVF) has been found with higher pregnancy-related distress compared with women with "naturally" achieved pregnancy. However, no difference has been found in level of attachment to their unborn children (9).

Features of children born via ART have also been investigated. Tully et al. (2003) (10) suggested that twins and triplets born after ART do not have any behavioral problems until age five, when compared with other "natural" multiple pregnancies. Colpin (2) concluded that 75% of parents who have children through ART do not mention about their ART process to their children, and children, whose parents declare these techniques to them, had more internalization problems. Infants conceived through IVF have slightly higher rates of major birth defects, longer duration of hospitalization, preterm birth, low birth weight and cerebral palsy (11). These medical conditions are other risk factors for psychological problems of the parents of ART children.

Studies on the mothers, who have children after ART, revealed no difference in supportive behaviors to their children compared with control group mothers, but these mothers found to be more protective of their children and more ignorant of their children's autonomy (2). However, Hahn and DiPietro (12) suggest that there is no difference between the two group mothers regarding the emotions and behavior towards their children. The results of the studies on psychological status and behavior of parents, who have children through ART, are controversial.

Studies that evaluate the psychosocial well-being of 9-18-year-old IVF children using the Child Behavior Checklist (CBCL), suggest that behavior and socioemotional functioning of these children are normal and there is no significant influence of IVF conception on behavior in adolescence (13,14). A review of studies on early development, cognition, and psychosocial well-being in children born after IVF suggest that, mental and psychomotor development during the first year and preschool years and cognitive development at 5 years are not deviant and at 6-12 years of age, no differences were observed in cognitive and school performance compared with naturally conceived children (15). No studies are available that evaluated cognitive aspects and school performance at secondary school age.

Krejcirova et al. (2008) (16) found that children who were born after intracytoplasmic sperm injection (ICSI) had higher rates of autism a finding which suggests that these children have to be followed up for social cognition problems during early childhood.

There are also several studies on psychosocial adaptation and emotional problems in children born via ART, but the number of studies on detailed psychiatric evaluations of these children are limited. On the other hand, Tully et al. reported that there was no difference between behavior of children born after ART and normal processes (10). The results of the studies on mental health of ART children are various and controversial.

In this study, our objective was to evaluate and compare the psychiatric diagnoses and the behavioral characteristics of children and adolescents born after ART with those of normally conceived ones. We also aimed to evaluate and compare the anxiety and depressive symptoms in mothers of ART children.

## Method

### Participants

In this cross-sectional study, we evaluated 35 children born after ART (ART group) and 35 naturally conceived children (control group), as well as their mothers. All children, whose application complaints were behavioral, academic and adjustment problems, anxiety and depressive symptoms, were recruited from the outpatient clinic of Child and Adolescent Psychiatry Department of Ege University School of Medicine (EUSM). 50 children were enrolled in the study group. All subjects provided written informed consent after a complete description of the study and study procedure. Eight parents of the study group refused to participate and forms of 7 parents had missing items. Thirty five children and their mothers completed the study. The control group (n=35) was comprised of age- and gender-matched naturally conceived children.

### Measurements

Socio-demographic characteristics of both samples were noted in a Socio-demographic Information Form established by the authors. ART and control groups were interviewed using Kiddie-Schedule for Affective Disorders and Schizophrenia (17,18). The Diagnostic and Statistical Manual of Mental Disorders, 4<sup>th</sup>. Edition (DSM-IV) criteria were used for psychiatric diagnoses (19). Developmental and mental capabilities of children were also evaluated by a clinical psychologist using the Ankara Developmental Screening Inventory (ADSI) for children younger than 6 years of age and the Wechsler Intelligence Scale for Children-Revised (WISC-R)-Turkish Version for children older than 6 years (20,21,22).

All mothers in both groups filled the CBCL for their children (23,24,25). Anxiety levels of the mothers were evaluated using the State-Trait Anxiety Inventory (STAI) and depression levels with the Beck Depression Inventory (BDI) (26,27,28,29).

Details of the assessment methods are given below:

**1) Sociodemographic Information Form:** Age, sex, familial characteristics, developmental stages and birth weights of the children are noted on this form.

**2) Kiddie-Schedule for Affective Disorders and Schizophrenia (K-SADS):** The K-SADS is a semi-structured interview to determine psychopathology in children and adolescents according to the DSM-IV criteria and was established by Kaufman et al. in (17). The Turkish adaptation study was made by Gokler et al. in (18).

**3) Child Behavior Checklist (CBCL):** The Turkish version of the CBCL is a self-administered parent-report questionnaire that contains 20 competence and 118 problem items. The competence scales are activity, social, and school. The problem scales are aggression, anxiety/depression, attention problems, delinquency, social problems, somatization, thought problems, and social withdrawal. The 118 problem items describe a wide array of problems that are rated on a 3-point scale. Parents score each item 0, 1, or 2 (not true, somewhat true, or very true, respectively). The test-retest reliability of the Turkish version was 0.84 for total problems, and the internal consistency was adequate (Cronbach's alpha= 0.88) (23,24,25).

**4) Spielberger's State-Trait Anxiety Inventory (STAI):** The State-Trait Anxiety Inventory (STAI-S/T) is a twenty-item self-report likert type scale for measuring anxiety that differentiates between the temporary condition of "state anxiety" (anxiety in a specific situation) and the more general and long-standing quality of "trait anxiety" (anxiety as a general trait) (26). Turkish adaptation study of the inventory was made by Öner and Le Compte (27). This inventory was used in this study to evaluate the anxiety levels of mothers.

**5) Beck Depression Inventory (BDI):** The BDI was developed by Beck et al. in 1961 and Turkish adaptation study was made by Hisli in 1988 (28,29). It includes 21 items to measure vegetative, emotional, cognitive and motivational symptoms of depression. Total score ranges between 0 and 63. A total score under 9 is interpreted as "no depression", 10-16 "mild depressive", 17-23 "moderate", and 24 and higher as "severe depressed". This inventory was used in this study for evaluating the depressive symptom levels in mothers.

**6) Childhood Autism Rating Scale (CARS):** The CARS was developed by Schopler and colleagues (30). It is used for the evaluation of autism and other pervasive developmental disorders. Turkish validation was made by Sucuoğlu et al. in (31). The scale rates the abnormality on a four-point scale with 15 items. In the present study, this scale was used for only subjects with pervasive developmental disorders, not for all cases.

**7) Ankara Developmental Screening Inventory (ADSI):** The ADSI is a 154-item scale widely used in Turkey for the assessment and evaluation of social, motor, cognitive, and communicative levels in children aged between 0 and 6 years (20). The total development score reflects the general development level of the child and it is obtained from the total of the four subscales (language-cognitive development, fine motor development, gross motor development, social interaction subscales).

**Table 1.** Sociodemographic features

	Study group (n=35)	Control group (n=35)	p
Age	5.34(±2.87)	5.34(±2.87)	1.000
Sex	13 girl 22 boy	13 girl 22 boy	1.000
Birth Weight	2378±703gr	3254±495gr	0.160
Singleton	8	17	0.022*
Twins	22	2	0.000*
Triplets	3	-	0.077
School Status	16 no attend to school 7 nursery 12 primary school	13 no attend to school 10 nursery 12 primary school	0.657

**8) Wechsler Intelligence Scale for Children-Revised (WISC-R):** The WISC-R is a standardized intelligence test for children and includes two parts, as verbal and performance subtests. The Turkish standardization was made by Savasir and Sahin in 1995 (21,22).

### Statistical Analysis

SPSS 16.0 for Windows was used for the statistical analysis. Current age of the mother, age at giving birth, psychiatric disorders ratios, CBCL score, BDI and STAI scores were evaluated with independent sample t-tests and chi-square to compare two groups (children born after ART/controls and their mothers). We considered p < 0.05 to be statistically significant. The age, gender and educational background of the subjects were analyzed with the frequency-analysis.

### Results

Thirty-five children (13 girls and 22 boys) were evaluated in ART group. The mean age of the ART children was 5.34±2.87 years (range: 2-13 years). The mean age of giving birth was 31.4±3.9. The mean birth-weight of the ART group was 2378±703 grams (range: 1050-3950 grams) and of the control group was 3254±495 grams (range: 1580-4300 gr). In the study group, 8 children were singletons and the control group included 17 singletons (p=0.022). The socio-demographic features of the children and adolescents are shown in Table 1.

There was no difference in overall psychiatric diagnosis rates between study and control groups (p=0.299). Only feeding disorders were found significantly higher in the study group compared to controls (p=0.020). Anxiety disorders were more common in ART group, but this tendency was not statistically significant. In ART group, five (14.3%) children had attention deficit and hyperactivity disorder (ADHD), five (14.3%) had pervasive developmental disorders (PDDs), one (2.9%) - autistic disorder, five (14.3%) - feeding disorder, six (17.1%) - anxiety disorder, three (8.6%) - obsessive compulsive disorder, three (8.6%) - mild developmental delay, two (5.8%) - major depressive disorder, one (2.9%) - psychogenic polydipsia and one (2.9%) subject had phonological disorder (Table 2).

**Table 2.** Psychiatric diagnoses of children (Study and control group)

Psychiatric Diagnoses	Study group		Control group		p
	n	%	n	%	
ADHD	5	14.3	7	20.0	0.526
PDDs	5	14.3	5	14.3	1.000
Autism	1	2.9	2	5.7	0.555
Feeding disorder	5	14.3	0	0.0	0.020 *
Anxiety disorder	6	17.1	4	11.4	0.495
Obsessive Compulsive Disorder	3	8.6	2	5.7	0.643
Major Depressive Disorder	2	5.7	1	2.9	0.555
Depressive disorder, NOS <sup>1</sup>	0	0.0	1	2.9	0.314
Psychogenic polydipsia	1	2.9	0	0.0	0.314
Phonological disorder	1	2.9	2	5.7	0.555
Language development delay	0	0.0	3	8.6	0.077
Mild developmental delay	3	8.6	2	5.7	0.643
Adjustment disorders	0	0.0	3	8.6	0.077
No psychiatric diagnosis	3	8.6	3	8.6	1.000
Total	35	100	35	100	

<sup>1</sup>Depressive disorder, not otherwise specified

\* p<0.05

**Table 3.** Comparison between mothers of both groups

	Mean±SD		t	df	p
	Study group n=35	Control group n=35			
Mothers' age	36.89±4.68	35.11±5.46	1.458	68	.149
Mothers' ages of childbearing	31.37±3.97	29.71±5.40	1.461	68	.148
BDI	13.26±7.76	7.54±7.98	3.036	68	.003*
STAI-S	46.51±13.13	37.17±11.80	3.132	68	.003*
STAI-T	48.86±9.73	38.86±9.67	4.315	68	.003*

\*p&lt; 0.05

**Table 4.** CBCL scores of both groups

	Mean±SD		t	df	p
	Study group n=35	Control group n=35			
Activity	40.46±6.54	41.04±4.92	-.359	50	.721
Socialization	41.23±6.91	42.65±6.66	-.756	50	.453
Withdrawn	58.77±10.15	52.27±3.07	3.126	29.53	.004*
Somatization	53.23±7.07	51.85±3.68	.886	37.65	.381
Anxiety/Depression	57.81±10.33	54.69±6.44	1.305	41.90	.198
Social Problems	57.12±8.84	52.85±5.38	2.103	41.26	.042*
Thought Problems	54.85±7.22	55.54±6.20	-.371	50	.712
Attention Problems	56.69±5.75	53.54±5.69	1.988	50	.052
Delinquency	52.31±5.57	51.85±4.61	.325	50	.746
Aggression	52.81±7.05	52.38±3.44	.275	36.27	.785
Internalization	54.62±12.36	47.96±11.05	2.046	50	.046*
Externalization	49.69±10.51	44.23±8.78	2.033	50	.047*
Total Problems	51.54±11.84	46.27±11.24	1.646	50	.106

\* p&lt; 0.05

Current age of the mothers and age at giving birth did not differ between the groups. When BDI and STAI scores of mothers of both groups were compared, mothers of the study group were shown to have statistically significant higher scores in both scales (study group BDI mean: 13.26, control group BDI mean: 7.54,  $p<0.05$ ; study group STAI-S mean: 46.51, control group STAI-S mean: 37.17;  $p<0.05$ ; STAI-T mean: 48.86, STAI-T mean: 38.86;  $p<0.05$ ) (Table 3).

Withdrawn, social problems and internalizing and externalizing subscale scores of CBCL were statistically significantly higher in study group than in control group (Table 4).

## Discussion

In this cross-sectional study, we compared the frequencies of psychiatric diagnoses and behavioral characteristics in children born after ART and those in naturally conceived children. The feeding disorder rate and CBCL subscale scores, such as withdrawn, social problems, internalizing and externalizing problems were higher in the study group. The most common

psychiatric diagnoses were ADHD, PDDs, and anxiety disorders in both groups. Since both groups were recruited from clinical samples, the diagnoses rates were similar to the findings of the study by Aras and colleagues, made in a clinical sample in Turkey, as expected (32). They also found ADHD, autism spectrum disorders and anxiety disorders as the most common diagnosis in the clinical population. The only different finding of our study was the frequency of the feeding disorders as it was found higher in our study group than in the control group. On the other hand, the psychiatric diagnosis rates in both groups were lower than in patient samples of the clinical studies made in USA, giving ADHD rates as 34% and depression 16% (33).

The studies on psychological and psychiatric outcomes of ART are limited and the results of these studies are various. Three children in our study group had mild developmental delay. There are studies which suggest that children born after ART (ICSI and IVF) have impaired cognitive development, but their IQ levels were not different when compared with controls (34,35). The high frequency of developmental delay (%8.6) in our study group was related to referral clinic (child psychiatry outpatient clinic) and cannot be related to ART. Nevertheless, there are also studies suggest that ICSI children had lower intellectual abilities compared to IVF children and, ICSI might be associated with the risk for a slightly delayed cognitive development compared to IVF (36).

Studies report that children born after administration of gonadotrophin-releasing hormone (GnRH) analogues in early pregnancy should be followed up for neurodevelopmental disorders, such as ADHD, motor development disorders, epilepsy, delayed language development (37). There are also studies suggest that ICSI may lead to autism and some other social cognition disorders (16,38). We also found that in the study group, 14.3% of children were with ADHD, 2.9% with autism and 14.3% of children were with PDD-S, but the difference between the groups was not statistically significant. These proportions are higher than the community sample rates, but similar to the findings of studies made in Turkish clinical samples (32). Similar to the findings of Knoester et al., our findings point to need for epidemiological studies to determine the prevalence of pervasive developmental disorders in children born via ART (38).

In the present study, 17% (n=6) of children were diagnosed as having anxiety disorder and %5.7 (n=2) major depressive disorder, a finding in line with results of Wagenaar et al. who suggested that children born after ART have more depressive and internalization symptoms (15). Internalization scores on CBCL were also significantly higher in the study group ( $p=0.046$ ) than in the control group. According to our knowledge, there are a limited number of studies performed a detailed psychiatric evaluation of children born from ART. It is important to determine the preventable and curable anxiety and depressive symptoms earlier in life, that these symptoms may be related to parental attitudes (39).

Another important finding of this study was the higher anxiety and depression levels in mothers of ART group children than in control mothers. It is important to evaluate the negative emotions of parents of children born from ART, since many studies reported high anxiety and emotional stress levels in women who experienced ART (2,3,4,5). It is known that, some psychopathologies in children

are highly related to psychiatric status of parents and parental attitudes. Thus, it is of great importance to deal with psychiatric symptoms of mothers of these children when treating anxiety and depressive symptoms of the children (39). On the other hand, high anxiety levels in ART mothers may lead them to overprotective parental attitudes and may cause to behave more protective to their children and ignorant of their children's autonomy, which may be an important etiological factor in feeding disorders of early childhood (2,7). The proposed link between maternal anxiety and feeding problems of a child may be important when our finding of the higher frequency of feeding disorder in the study group is regarded.

Prematurity and low birth weight are considered as risk factors for feeding disorders and babies may have eating problems if they do not get enough breastfeeding (7). The number of singletons in the ART group was significantly less than in the control group, similar to the studies that found high rates twin births resulting from ART (40).

Anxiety levels in mothers were found to be higher in ART group in our study. High anxiety levels in mothers may also trigger feeding disorders in children (7). Depressive and anxiety symptoms of parents, having a "special" baby and previous losses of pregnancies may be various causes of feeding disorders in children. Working with anxiety and depression of parents and parental attitudes may cure feeding disorders, and this is an important area for working on coping strategies for feeding disorders in this special group of children (children born with ART) (7).

Although one can expect that mothers who had children through ART would be older than the controls current age of the mother or the age at giving birth did not differ between groups. This finding can be related to lifestyle of traditional families in Turkey as the couples want to have a baby in the early years of their marriage, and if they cannot conceive a baby naturally, they may try ART. There are studies reported having old parents is a risk factor for anxiety, depressive and aggressive behavior in children (41).

In a non-clinical sample by Wagenaar et al. (13) CBCL scores of IVF children versus controls were found to be lower on the total problems scale, externalizing scale and syndrome scales thought problems, attention problems, aggressive and rule-breaking behavior. As a result, Wagenaar et al. suggested that 9-18-year-old IVF children are normal regarding behavioral and socio-emotional functioning. However, we found that CBCL subscale scores (i.e. withdrawn, social problems, internalizing and externalizing problems) in the study group were higher than in the control group. There may be two possible explanations for these discrepant findings; first the sample size of our study was smaller than the study of Wagenaar et al. that may have led to type I error. Second, as we had a clinical sample, our study may have been flawed by a referral bias. Although studies which emphasize on negative effects of these techniques, high scores found in the subscales need to be reassessed in future studies as there are studies on long-term mental health of children born after ART have controversial results.

#### Limitations

The main limitation of the study was the sampling of the control group as the control group comprised of children who were referred to the Child and Adolescent Psychiatry outpatient unit. This sampling bias may have led to the similar frequencies of psychiatric

disorders in both groups except for the feeding disorders. However, despite the sampling bias, we suggest that the high frequency of feeding disorders in ART children is an important finding. Nevertheless, our findings should be interpreted with caution because of the small sampling size which is the second important limitation of the study.

For determination of the effect of ART on children psychiatric status, recruiting a larger group of children born after ART from the community can be planned for future studies. Collaborative studies with other clinics like pediatric clinics or infertility and ART departments of gynecology clinics may also give a chance to understand this group of children.

#### Summary:

In this study we evaluated a clinical sample of children born after ART and noted various psychiatric diagnoses. According to our knowledge, this preliminary study was the first study on psychiatric diagnosis and behavioral symptoms of children born after ART in Turkey. Since there are limited studies on this area, evaluation of the psychiatric status of these children and parents will be helpful for clinicians in the management of this population and will contribute to preventive mental health attempts.

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