

# Psychiatric Consultations and Treatment Adherence in Pediatric Solid Organ Transplant Recipients: The Role of Adjustment Disorder

*Pediatric Katı Organ Nakli Alıcılarında Psikiyatrik Konsültasyonlar ve Tedaviye Uyum: Uyum Bozukluğunun Rolü*

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## ABSTRACT

**Objectives:** This study aims to examine the clinical characteristics of pediatric solid organ recipients who underwent consultations with the child and adolescent psychiatry department. Additionally, it seeks to identify predictive factors associated with non-adherence to treatment, as reported by the transplant center, during their hospitalization.

**Materials and Methods:** All solid organ transplant recipients under the age of 18, who were inpatients at Başkent University Hospital Transplant Center between August 2012 and August 2023, and who underwent consultation with the Department of Child and Adolescent Psychiatry, were included in the study. Data was collected retrospectively from hospital records.

**Results:** The study cohort consisted of 55 solid organ transplant recipients, including children with a mean age of 10.3±4.34 years who underwent kidney, liver, and heart transplants. Following the psychiatric examination, the most common diagnosis (50.9%) was adjustment disorder (AD). Within this diagnosis, the most frequently observed subtype was “with depressive mood” (39.3%). Additionally, non-adherence to treatment was reported in 27.3% of these patients. It was determined that the diagnosis of AD was an independent predictor of non-adherence to treatment (odds ratio: 15.77, 95% confidence interval: 1.77-140.75, p=0.014).

**Conclusion:** The results emphasize the vital role of child and adolescent psychiatry consultations in the post-transplant period, shedding light on the diagnosis of AD as a crucial factor in predicting non-adherence to treatment in these patients.

**Keywords:** Transplantation, adjustment disorder, child, adolescent

## ÖZ

**Amaç:** Bu çalışmada çocuk psikiyatrisi bölümüne konsültasyonu yapılan, solid organ nakilli çocukların klinik özelliklerinin incelenmesi; ayrıca hastanede yattığı süreçte, nakil merkezi tarafından bildirilen tedaviye uyumsuzluğun risk faktörlerinin belirlenmesi hedeflenmiştir.

**Gereç ve Yöntem:** Çalışmaya Başkent Üniversitesi Hastanesi Nakil Merkezi'nde Ağustos 2012 ile Ağustos 2023 tarihleri arasında yatan, Çocuk ve Ergen Psikiyatrisi Bölümü'ne konsültasyonu yapılan, 18 yaş altı tüm katı organ nakli alıcıları dahil edildi. Veriler hastane kayıtlarından geriye dönük olarak toplandı.

**Bulgular:** Çalışma kohortu yaş ortalaması 10,3±4,34 olan 55 katı organ (böbrek, karaciğer ve kalp) nakilli çocuktan oluşmaktadır. Ruhsal muayene sonucunda en sık (%50,9) konulan tanı uyum bozukluğu (UB) iken; bu tanının içinde “depresif duygudurum ile giden” en sık gözlemlenen alt tip oldu (%39,3). Ayrıca bu hastaların %27,3'ünde tedaviye uyumsuzluk raporlanmış; UB tanısının tedaviye uyumsuzluğun bağımsız bir yordayıcısı olduğu belirlenmiştir (odds oranı: 15,77, %95 güven aralığı: 1,77-140,75, p=0,014).

**Sonuç:** Bulgular nakil sonrası dönemde çocuk ve ergen psikiyatrisi konsültasyonlarının hayati rolünü vurgulayarak, bu hastalarda tedaviye uyumsuzluğunu öngörmeye önemli bir faktör olan UB tanısına ışık tutmaktadır.

**Anahtar Kelimeler:** Transplantasyon, uyum bozukluğu, çocuk, ergen

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## Introduction

Due to swift advancements in the field of medicine, organ transplantation has emerged as a crucial treatment for enhancing both survival rates and quality of life.<sup>1</sup> Given that the 5-year survival rates for solid organ transplants have reached approximately 80%, healthcare professionals are focusing on augmenting quality of life during the post-transplant period.<sup>2-4</sup>

After transplantation, a multitude of factors come together, representing a crucial intersection that can impact the mental health of children. This period entails physical recovery and significant changes, ranging from family dynamics to school life and social relationships. Various determinants impact the mental well-being of children and adolescents during the post-transplant period. These factors comprise diverse elements, encompassing physical appearance, health-related considerations, adjustment to the novel lifestyle and treatment protocols, academic anxieties, and complexities in interpersonal relationships with friends and family.<sup>5</sup> All these factors challenge children's capacity to uphold mental equilibrium. Researchers consistently note that, throughout the post-transplant period, children manifest a diminished quality of life in comparison to their healthy counterparts, particularly across overall functionality, physical and psychosocial well-being, and social and academic performance.<sup>6,7</sup> Moreover, heightened prevalence rates of psychiatric disorders, including anxiety, depression, and adjustment disorders (AD), have been substantiated among these children.<sup>8-10</sup>

After organ transplantation, consistent adherence to immunosuppressants is crucial for preserving the transplanted organ's functionality and reducing the risk of rejection.<sup>11</sup> Nevertheless, scholarly investigations posit that psychiatric disorders may serve as contributory factors to treatment non-adherence, consequently resulting in heightened levels of morbidity and mortality.<sup>8,10,12</sup> Statistical approximations indicate that the prevalence of non-adherence to immunosuppressive drugs ranges between 50-65% among pediatric transplant recipients, with an increased risk observed during the transitional phase of adolescence.<sup>13,14</sup>

While numerous studies have explored the psychological well-being of adults in the post-transplantation phase, our understanding of the mental state of children and adolescents in this context remains limited. The primary objective of this study is to examine the clinical attributes of pediatric transplant recipients and identify factors that predispose them to treatment non-adherence at the transplant center. The anticipated outcome of this research is to provide valuable insights that will help shape mental health protective services within pediatric consultation-liaison psychiatry.

## Materials and Methods

This study received approval from the Başkent University Institutional Review Board and Ethics Committee (project no: KA23/291, date: 22.08.2023) and was conducted according to the principles of the Declaration of Helsinki. All solid

organ transplant recipients under the age of 18 who received inpatient treatment at Başkent University Hospital Transplant Center and had consultations with the Department of Child and Adolescent Psychiatry between August 2012 and August 2023 were included in the study. Data were retrospectively collected from hospital records in August 2023. The study assessed patients' socio-demographic characteristics, medical conditions, treatment adherence, psychiatric histories, and the use of psychotropic drugs. In cases involving recurrent consultations, the last consultation before discharge was considered. Non-adherence to treatment is defined as the rejection of treatment protocols recommended by the transplant center during the hospital stay or the need for intense effort from the medical staff to ensure compliance. According to our hospital's standard protocol, psychiatric consultation is requested for children hospitalized during the post-transplant period in instances of treatment non-adherence and/or suspicion of mental health problems. Children who undergo consultation are administered a comprehensive mental status examination by a specialized child and adolescent psychiatrist. The diagnosis of psychiatric disorders is established through rigorous clinical evaluation.

## Statistical Analysis

The data analysis utilized IBM SPSS version 25 (IBM Inc., Armonk, NY) software. Data distribution was assessed with the Shapiro-Wilk test. Descriptive statistical analyses were conducted, and group comparisons were executed using appropriate statistical tests, such as the Mann-Whitney U test, Pearson's chi-square test, or Fisher's exact test, depending on the characteristics of the variables and the data. To identify factors predicting non-adherence treatment in children, logistic regression analysis was applied. Variables with a p-value below 0.2 in the univariable analyses were included in the model using the "Enter" method. Before analysis, an assessment of logistic regression assumptions was performed. Statistical significance was set at a p-value threshold of less than 0.05.

## Results

### Descriptive Statistics

Over 11 years, a total of 55 recipients of organ transplants underwent consultations with the department of child and adolescent psychiatry. Among them, 40% (n=22) were male, while 60% (n=33) were female, with a mean age of 10.3 [standard deviation (SD): 4.34]. Within this cohort, 32.7% (n=18) were recipients of kidney transplants, 54.5% (n=30) received liver transplants, and 12.7% (n=7) underwent heart transplantation. These children were diagnosed with a psychiatric disorder at a mean age of 3.77 (SD: 4.51) and underwent organ transplantation at a mean age of 8.05 (SD: 4.65). Among the patients, 14.5% (n=8) had a previously diagnosed neurodevelopmental disorder (NDD), encompassing six cases of intellectual disability (ID), one case of attention deficit hyperactivity disorder, and one case involving both ID and autism spectrum disorder. Upon scrutinizing the reasons for consultations, it was identified that depressive symptoms were the most prevalent (29.1%),

followed by irritable/destructive behaviors (21.8%) and anxiety symptoms (10.9%).

Moreover, throughout the hospitalization period, healthcare professionals at the transplant center reported that 27.3% of these patients demonstrated treatment non-adherence. After the consultations, psychiatric disorders were diagnosed with 83.6% of the patients (refer to Table 1). The predominant diagnosis was AD at 50.9%, followed by major depressive disorder (MDD) at 9.1%. Within the AD category, the most frequently identified subtype was “AD with depressed mood” (39.3%), succeeded by “AD with disturbance of conduct” (28.6%), “AD with anxiety” (21.4%), “AD with mixed disturbance of emotions and conduct” (7%), and “AD with mixed anxiety and depressed mood” (3.6%). In terms of gender distribution, “AD with depressed mood” was more prevalent among girls (21.2%), while among boys, “AD with disturbance of conduct” was observed at a rate of 22.7%.

Psychotropic drug treatment was initiated in 63.6% of the children. The most prescribed medications were selective serotonin reuptake inhibitors (45.6%), including sertraline (20%), escitalopram (17%), and fluoxetine (8.6%), and haloperidol (40%). Less frequently utilized medications included risperidone (11.4%), hydroxyzine (15.7%), clonazepam (2.9%), and quetiapine (2.9%). The primary reason for initiating medications was the diagnosis of AD (60%).

#### A Comparison Between the Adherence and Non-adherence Treatment Groups as Reported by Healthcare Professionals

Following descriptive analyses, an exploration of potential risk factors associated with treatment non-adherence was undertaken. To achieve this objective, a comparison was made between patients who exhibited treatment non-adherence and those who adhered to treatment. Variables such as age, gender, organ type, age at the time of medical illness diagnosis, time interval since diagnosis, age at the time of transplantation, time

interval since transplantation, and the presence of AD, MDD, generalized anxiety disorder (GAD), and NDD were considered in this comparison (refer to Table 2). As a result, treatment non-adherence was noted in 46.4% of children diagnosed with AD and 7.4% of children without AD. The difference in the frequency of treatment non-adherence based on the presence of AD was found to be significant between the groups;  $\chi^2(1)=10.55$ ,  $p<0.001$ . Furthermore, within the treatment non-adherence group, the time interval since diagnosis was observed to be shorter ( $U=175$ ,  $p=0.018$ ). However, no significant differences were observed between the groups in terms of other variables (Table 2).

#### Predictors of Treatment Non-adherence as Reported by Healthcare Professionals

A logistic regression analysis was conducted to identify characteristic features of treatment non-adherence, as reported by healthcare professionals, in patients who received consultations from child and adolescent psychiatry. In this analysis, variables from univariable analyses with a p-value below 0.2 were included as independent variables in the model (Table 3). These variables included the presence of AD, MDD, or GAD, age at the time of medical illness diagnosis, and the time interval since diagnosis. Before performing the analysis, assumptions of logistic regression were examined. The correlation coefficients between variables were all found to be below 0.9. The variance inflation factor values were below five, and tolerance scores were above 0.2, indicating the absence of multicollinearity issues. Cook’s distance was examined to identify outliers, but no value greater than one was observed. Therefore, the analysis met the assumptions of regression. The resultant model explained 37.6% of the variance ( $\chi^2=16.54$ , degrees of freedom =4,  $p=0.002$ ). Consequently, the presence of AD was established as an independent predictor of treatment non-adherence (odds ratio: 15.77, 95% confidence interval: 1.77-140.75,  $p=0.014$ ).

#### Discussion

In this study, AD, characterized by emotional and behavioral symptoms in response to stressors, emerged as the most prevalent mental health concern among pediatric solid organ transplant recipients who underwent consultations in child and adolescent psychiatry (50.9%). Additionally, it was determined that AD served as a risk factor for treatment non-adherence in pediatric solid organ transplant recipients. This significant observation underscores the imperative for comprehensive psychiatric support within the transplantation center.

The intricate interplay between physical health and psychological well-being has long been acknowledged, particularly in the realm of pediatric solid organ transplantation.<sup>13</sup> Following the transplant, transplant recipients and/or caregivers are required to adhere to a medical regimen that encompasses lifelong immunosuppressant medication, regular checkups, and laboratory testing.<sup>15</sup> The considerable burden of a life-altering

**Table 1. Psychiatric disorders diagnosed in the study population**

Psychiatric disorders	Number of patients, (%)
Adjustment disorder	28 (51%)
With depressed mood	11 (20%)
With disturbance of conduct	8 (14.5%)
With anxiety	6 (10.9%)
With mixed disturbance of emotions and conduct	2 (3.6%)
With mixed emotions	1 (1.8%)
Major depressive disorder	5 (9.1%)
Delirium	3 (5.5%)
Generalized anxiety disorder	2 (3.6%)
Obsessive-compulsive disorder	2 (3.6%)
Autism spectrum disorder	2 (3.6%)
Trichotillomania	2 (3.6%)
Intellectual disability	1 (1.8%)

procedure, combined with the requirement for ongoing medical vigilance, can catalyze emotional turmoil. The emotional upheaval accompanying this condition can hinder treatment adherence, thereby potentially compromising the fragile mental equilibrium. Our findings underscore the importance of comprehending and addressing these emotional challenges as integral to comprehensive transplant care.

Studies conducted during both the pre-transplant and post-transplant periods have reported that AD is a prevalent psychiatric disorder in these children.<sup>16,17</sup> In another study conducted during the pre-transplant period for children at the same center, AD was identified as the most frequently diagnosed condition.<sup>18</sup> The study revealed that being a candidate for heart transplantation, as opposed to liver or kidney transplantation, and experiencing prolonged hospital stays both increased the risk of AD. In addition, longitudinal studies have reported

that AD predicts future major psychiatric disorders, with a 3.4 times higher risk of developing such disorders in the AD group compared to controls.<sup>19,20</sup> Consistent with the literature, the most prevalent subtype of AD in this sample was “with depressed mood”; among males, the most frequent subtype was “with disturbance of conduct”. While this study observed that AD was the most prevalent cause of psychotropic usage among inpatients during the post-transplant period, there remains a lack of consensus in the literature concerning the treatment and management of AD.<sup>21,22</sup> However, some authors argue that unnecessary drug usage for AD should be avoided, as these disorders often improve naturally once the underlying stressors dissipate.<sup>22,23</sup> Even though AD represents one of the most commonly utilized diagnoses in consultation-liaison psychiatry,<sup>24,25</sup> there is a requirement for longitudinal studies to address the existing gaps in the literature regarding the management and treatment of AD.

**Table 2. Comparison between treatment adherence and non-adherence groups**

Parameters		Treatment adherence (n=40) n (%) / median (IQR)	Treatment non-adherence (n=15) n (%) / median (IQR)	p-value
<b>Age (year)</b>		10.21 (7.48)	11.83 (8.50)	0.664 <sup>c</sup>
<b>Gender</b>	Female	26 (78.8%)	7 (21.2%)	0.216 <sup>a</sup>
	Male	14 (63.6%)	8 (36.4%)	
<b>Organ type</b>	Liver	21 (70%)	9 (30%)	0.839 <sup>a</sup>
	Kidney	14 (77.8%)	4 (22.2%)	
	Heart	5 (71.4%)	2 (28.6%)	
<b>Age at diagnosis (year)</b>		0.96 (4.75)	6.0 (11.17)	0.119 <sup>c</sup>
<b>Time interval since diagnosis (year)</b>		6.88 (4.69)	3.0 (5.33)	0.018 <sup>c</sup>
<b>Age at transplantation (year)</b>		7.04 (7.43)	8.0 (8.0)	0.411 <sup>c</sup>
<b>Time interval since transplantation (year)</b>		0.96 (4.44)	0.92 (3.75)	0.387 <sup>c</sup>
<b>NDD</b>	Absent	32 (72.7%)	12 (27.3%)	0.658 <sup>b</sup>
	Present	8 (72.7 %)	3 (27.3%)	
<b>AD</b>	Absent	25 (92.6)	2 (7.4%)	<b>0.001<sup>a</sup></b>
	Present	15 (53.6%)	13 (46.4%)	
<b>MDD/GAD</b>	Absent	33 (70.2%)	14 (29.8)	0.423 <sup>b</sup>
	Present	7 (87.5 %)	1 (12.5%)	

Note: Bold values correspond to statistically significant. Data presented as number (%) and median (IQR) as appropriate. <sup>a</sup>Pearson chi-square test was used, <sup>b</sup>Fisher Exact test p-value, <sup>c</sup>Mann-Whitney U test was used.

NDD: Neurodevelopmental disorder, AD: Adjustment disorder, MDD/GAD: Major depressive disorder/generalized anxiety disorder

**Table 3. Logistic regression analysis for treatment non-adherence**

Parameters	B	SE	Wald	df	p-value	Exp (B)	(95% CI)
Age at diagnosis	0.09	0.09	1.05	1	0.306	1.10	(0.92-1.31)
Time interval since diagnosis	-0.106	0.109	0.95	1	0.328	0.90	(0.73-1.11)
Adjustment disorder (0: Absent)	2.76	1.12	6.10	1	<b>0.014</b>	15.77	(1.77-140.75)
MDD/GAD (0: Absent)	1.63	1.56	1.10	1	0.294	5.12	(0.24-108.01)

Note: Bold values correspond to statistically significant.

B: Beta, SE: Standart error, df: Degrees of freedom, OR: Odds ratio, CI: Confidence interval, MDD/GAD: Major depressive disorder/generalized anxiety disorder

Within the literature, reports indicate that non-adherence to treatment is more prevalent during adolescence than in younger children and adults, and that AD tends to manifest with greater severity among adolescents.<sup>26-30</sup> Furthermore, this pattern is notably more prominent among individuals grappling with psychiatric disorders, including but not limited to depression, anxiety disorders, and post-traumatic stress disorder (PTSD).<sup>31</sup> However, the current study did not establish a significant association between treatment non-adherence and age, nor between it and other mental illnesses. This lack of correlation was attributed to the limitations in the study's sample size.

### Study Limitations

The study's outcomes necessitate careful consideration within the context of certain limitations. Primarily, it is crucial to recognize that the nature of this investigation, being cross-sectional and retrospective, precludes the establishment of causal relationships among the variables under scrutiny. Moreover, the study's scope is limited by the relatively small sample size of its participants. Furthermore, the generalizability of the findings is constrained by the fact that the sample exclusively comprises a subset of individuals referred to for consultation within the domain of child psychiatry. A further constraint pertains to the diagnostic process for mental health conditions, which relies on clinical assessments conducted by child and adolescent psychiatrists. Additionally, the assessment of treatment adherence relied on subjective evaluations provided by the transplant center's healthcare team, without using a standardized measurement scale. These limitations collectively underscore the need for prudence when interpreting and extrapolating the study's outcomes.

### Conclusion

The prediction of treatment non-adherence in AD sheds light on the necessity of tailored intervention strategies. Developing a comprehensive treatment approach that includes psychological assessment and therapeutic support for adherence could be crucial in overcoming the barriers posed by emotional distress. By integrating transplant and psychiatric expertise, healthcare teams can create an environment where treatment adherence becomes a collaborative endeavor, fostering the physical and emotional well-being of pediatric transplant recipients. In conclusion, our study highlighted the significance of AD in pediatric solid organ recipients and prompted a reevaluation of the psychiatric dimensions of transplant care.

### Ethics

**Ethics Committee Approval:** This study received approval from the Baskent University Institutional Review Board and Ethics Committee (project no: KA23/291, date: 22.08.2023) and was conducted according to the principles of the Declaration of Helsinki.

**Informed Consent:** Informed consent not available due to retrospective design.

### Footnotes

#### Authorship Contributions

Concept: D.K., Design: D.K., Data Collection or Processing: D.K., B.A.S., H.A.T., Analysis or Interpretation: D.K, Literature Search: D.K., B.A.S., H.A.T., Writing: D.K., B.A.S., H.A.T.

**Conflict of Interest:** The authors declare no conflicts of interest.

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