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Editor
Melis Palamar, MD
Ege Universitesi Tip Fakultesi, Goz Hastaliklari AD, Bornova, Izmir, Türkiye
Tel: +90 232 390 37 88
melispalamar@gmail.com

Contact – Publishing House:
Kare Publishing - Kare Media
Goztepe Mah. Fahrettin Kerim Gokay Cad. No: 200 Da: 2, Goztepe, Kadikoy, Istanbul, Türkiye
Phone: +90-216-550 61 11 Fax: +90-216-550 61 12
e-mail: kare@karepb.com Web: kare@karepb.com

Publications Coordinator: Burak Türe
Graphic Design: Beste Kurtcu Ay

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CONTENTS

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EDITORIAL

Dear Readers,

We are glad to introduce European Transplant Research, a brand new academic journal on advancing knowledge and innovation in the field of organ and tissue transplantation.

The primary mission of European Transplant Research is to provide an open access platform for sharing high-quality, peer-reviewed articles to address the challenges and opportunities of transplantation. The journal welcomes original research articles, reviews, case reports, and short communications that contribute to transplant procedures, transplant immunology, graft preservation, and post-transplant care.

With European Transplant Research, we aim to push the boundaries of transplantation science, facilitate the exchange of ideas, and ultimately contribute to the advancement of global healthcare standards. We invite authors, reviewers, and readers to join us in this endeavor and look forward to a dynamic and impactful journey ahead.

The articles accepted are now available online. You might check the psychiatric aspects of pediatric transplant patients as well as nursing approaches in immunosuppressive medication adherence. You might as well read about a health-care problem – topical anesthetic abuse keratopathy – that is to be solved with corneal transplant surgery.

On behalf of the editorial board, we welcome you to European Transplant Research and anticipate a future filled with groundbreaking discoveries and meaningful contributions to the field.

Melis Palamar,

Chief Editor

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EUROPEAN TRANSPLANT RESEARCH

ORIGINAL ARTICLE

Psychiatric and psychosocial characteristics of pediatric transplantation candidates-evaluation scale

Nazlı Burcu Özbaran,[1] Seda Erbaş,[2] Zeynep İrem Erbasan,[1] Tuğçe Özcan,[3] Mediha Korkmaz[4]

[1]Department of Child and Adolescent Psychiatry, Ege University Faculty Of Medicine, Izmir, Turkiye
[2]Department of Child and Adolescent Psychiatry, Gaziantep City Hospital, Gaziantep, Turkiye
[3]Department of Child and Adolescent Psychiatry, Isparta City Hospital, Isparta, Turkiye
[4]Department of Psychology, Ege University, Izmir, Turkiye

Abstract

Introduction: This study aimed to standardize psychiatric assessments for organ transplant candidates by developing a semi-structured interview tool to ensure consistent evaluations and protective measures.

Methods: The study included 34 pediatric solid organ transplant candidates: 8 pre-school, 10 pre-adolescent, and 16 adolescent patients. All participants were evaluated independently by two clinicians. The Psychiatric and Psychosocial Characteristics of Pediatric Transplantation Candidates–Evaluation Scale (PPCPT-ES), the Satisfaction with Life Scale for Children, and the Hope in Children Scale were administered to all patients. Item analysis and internal consistency reliability analyses were conducted separately for both raters across the 18 items of the PPCPT-ES.

Results: Four items were excluded from the analysis: three due to item–total score correlation values below 0.20 and one due to lack of significance in the interrater consistency analysis. For the remaining 14 items, item–total score correlation values ranged from 0.29 to 0.72 for rater 1 and from 0.25 to 0.70 for rater 2. The internal consistency reliability coefficient (Cronbach's alpha) was 0.86 for both raters.

Discussion and Conclusion: These findings suggest that the PPCPT-ES demonstrates good internal consistency and measures a homogeneous construct as a continuous variable, supporting its potential utility in the standardized psychiatric assessment of pediatric organ transplant candidates.

Keywords: Multidisciplinary, pediatric, psychiatry, scale, transplantation.

Transplantation is a multidisciplinary treatment involving the transfer of living cells or tissues from a donor to a recipient, allowing them to function in the new host [1].

The pre-transplant period poses stressors for young transplant patients, involving physical and psychosocial challenges stemming from chronic illness. These include concerns about functional loss due to health status, dependency on others for daily tasks, worries about suitability for transplantation, prolonged waiting periods, and fears about survival until the transplant. The primary aim of pre-transplant psychosocial assessment is to identify physiological or psychosocial traits that could adversely impact post-transplant outcomes [2]. In pre-transplant psychiatric assessment for children and adolescents, various

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Correspondence: Seda Erbaş, M.D. Department of Child and Adolescent Psychiatry, Gaziantep City Hospital, Gaziantep, Turkiye
E-mail: sedaerbas@yahoo.com
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factors influencing transplantation success—including psychosocial status, psychiatric history, medication use, substance history, cognitive abilities, and understanding of transplantation processes—are thoroughly examined [3-6].

Following eligibility for transplantation, the transition from waiting to transplantation is a mixed experience for patients and their families, encompassing moments of joy alongside anxiety, fear, and stress due to entering a new phase [7]. Hospitalization procedures, transplantation-related processes, medical interventions, and intensive care stays can be emotionally challenging for both patients and their families [6]. Anxiety disorders are the most prevalent psychopathologies observed during this phase [8]. Child and Adolescent Psychiatry plays a crucial role in providing psychosocial support, assessing psychiatric conditions, arranging necessary treatments for identified psychopathologies, and monitoring mental changes resulting from organic causes.

Psychiatric challenges may persist post-transplant in pediatric and adolescent cases. A 2005 study with 104 transplant patients reported that 30.7% exhibited posttraumatic stress disorder symptoms [9]. A 2022 study reported a 9.2% prevalence of posttraumatic stress disorder [10]. A 2011 study found that mental health problems can persist for years after pediatric kidney transplantation, negatively affecting recipients' quality of life [11]. Similarly, a 2020 article highlighted depression, anxiety, developmental delays, and learning difficulties in young kidney transplant recipients [11]. A study comparing liver transplant patients with healthy controls revealed more emotional and behavioral problems in the transplant group [12]. Pediatric heart and lung transplant patients may also experience depressive symptoms, anxiety, behavioral challenges, and somatic complaints during adaptation to the disease and its treatment [13].

In the literature, standardized pre-transplant psychosocial risk assessment tools have been deemed valuable for enhancing transplant success when combined with tailored multidisciplinary interventions introduced early in the transplantation process [14]. Assessment instruments such as the Stanford Integrated Psychosocial Assessment for Transplantation (SIPAT), Structured Interview for Renal Transplantation (SIRT), Transplant Evaluation Rating Scale (TERS), and Psychosocial Assessment of Candidates for Transplantation (PACT) are primarily applicable to adult patients [15-18].

The Pediatric Transplant Rating Instrument (P-TRI) is a 17-item scale developed to evaluate psychosocial risk factors for adverse prognosis after solid organ transplantation [19]. The Turkish version of the P-TRI has demonstrated good psychometric properties for pediatric kidney transplant recipients. To our knowledge, no comprehensive psychosocial assessment tool exists for pediatric solid organ transplant candidates in Türkiye, aside from the Turkish adaptation of the P-TRI for kidney transplant candidates.

Highlights

- PPCPT-ES is a comprehensive scale originally consisting of 18 items that address common psychosocial risk domains
- PPCPT-ES demonstrated strong psychometric properties, including high internal consistency and inter-rater reliability
- PPCPT-ES has potential utility for predicting treatment compliance in pediatric transplant candidates prior to surgery

The primary aim of psychiatric evaluation in pediatric organ transplantation is to select suitable recipients and donors, inform and support patients and families, detect mental health issues in the pre-transplant, transplant, and post-transplant phases, provide early intervention to prevent organ rejection, and enhance the individual's adaptation and quality of life. Varied global guidelines on psychiatric disorders as contraindications highlight the need for individualized, multifactorial evaluations, recognizing potential differences in processes and outcomes. Some studies categorize the presence of psychiatric disorders as either definite contraindications (e.g., dementia, acute psychosis, drug or alcohol dependence, highly unstable borderline personality disorder, IQ <70) or relative contraindications (e.g., therapeutic incompatibility, personality disorders, depression, anxiety disorders, lack of motivation for the procedure). Others argue that a psychiatric disorder alone does not necessarily constitute a contraindication to organ transplantation. Emphasis has therefore been placed on the importance of individualized, multifactorial evaluations, acknowledging potential variations in processes and transplant success on a case-by-case basis [20-24].

Given the numerous factors influencing both short- and long-term transplantation outcomes, pre-transplant risk assessment is crucial. Standardized assessment tools in pediatric populations are believed to aid in identifying risks, guiding psychosocial support, and predicting outcomes, thereby facilitating appropriate interventions.

This study aimed to standardize psychiatric evaluation for pediatric organ transplant candidates by determining their biological, individual, familial, social, and economic

challenges; identifying existing psychopathologies; and providing appropriate pharmacological and psychosocial support. The study further sought to identify patients at risk of psychiatric and psychological difficulties during the transplantation process and post-transplant period, and to develop a semi-structured interview tool to standardize psychiatric evaluation and implement necessary protective measures.

Materials and Methods

This study was approved by the Ege University Faculty Of Medicine University Medical Research Ethics Committee (Approval No: 22-1T/11, Date: 14.01.2022) and conducted between January 2022 and August 2023 in the Department of Child and Adolescent Psychiatry, Ege University Faculty of Medicine Hospital. The study focused on scale development using correlational methods to examine relationships between scale items.

The research was carried out as part of the multidisciplinary team working in the pre-transplant, transplant, and post-transplant phases, and specifically included solid organ transplant patients followed at the Department of Child and Adolescent Psychiatry, Ege University. The study was supervised by a permanent faculty member. All procedures were conducted in accordance with the principles of the Declaration of Helsinki.

Sample Group

The study included all transplant candidates aged 0–18 who were referred to the Department of Pediatric and Adolescent Psychiatry for pre-transplant psychiatric evaluation. Informed consent was obtained from both candidates and their parents prior to participation. Psychiatric interviews were conducted either at the bedside in patient rooms or in psychiatric outpatient clinics, depending on the clinical condition and age of the transplant candidates. Age-appropriate one-on-one sessions were held with the candidates and their parents.

A consultant psychiatrist used a semi-structured interview tool based on DSM-5 criteria for psychiatric diagnoses and scored items on the Evaluating Psychiatric and Psychosocial Characteristics of Pediatric Transplantation Candidates Interview Form. Two expert assessors were present during the interviews, with one conducting the interview and the other independently scoring on a separate PPCPT-ES form. Given the rarity of pediatric solid organ transplant candidates, no a priori power analysis was performed. Instead, all eligible cases referred to the department for psychiatric consultation over a one-year period were included, consistent with approaches used in prior psychosocial instrument development studies involving pediatric transplant populations.

Inter-rater reliability—assessing agreement between raters—was a central focus in this scale development study. The PPCPT-ES items were scored on a continuous scale (0–10), with the last four items reverse-scored. Inter-rater reliability was determined using the intraclass correlation coefficient (ICC), ranging from 0 to 1. High ICC values indicated strong agreement between raters, whereas values near zero suggested a lack of agreement [25, 26]. Each participant was evaluated by two consultant psychiatrists, generating multiple measurements. Average agreement values were calculated by assessing consistency across these measurements [27].

For age-specific assessments, the Satisfaction with Life Scale for Children and PPCPT-ES were administered to patients aged 8–13, the Hope in Children Scale and PPCPT-ES to those aged 8–16, and only the PPCPT-ES to patients younger than 8 years.

Assessment Tools

Satisfaction with Life Scale for Children

Developed by Gaderman, Reichl, and Zumbo, this tool is a valid and reliable measure of life satisfaction [28]. It consists of 5 items with a single-factor structure, each rated on a 5-point Likert scale. The scale is designed for children aged 8–13. It was adapted into Turkish by Altay and Ekşi [29].

Children's Hope Scale

The Hope in Children Scale was developed by Snyder et al. in 1997 [30]. The scale includes 6 items rated on a Likert scale. Scores are obtained by summing item responses, with a minimum of 6 and a maximum of 36. It is suitable for children aged 8–16. The Turkish adaptation was conducted by Atik and Kemer [31].

Evaluating Psychiatric and Psychosocial Characteristics of Pediatric Transplantation Candidates Interview Form

This form was created by child and adolescent psychiatry specialists and includes 4 main headings and 5 subheadings. It gathers information about the medical disease process, transplantation process, psychiatric evaluation, patient and parent substance use history, treatment compliance, family environment, financial and psychosocial support, relationships with the medical team, and the patient's cognitive capacity.

Psychiatric and Psychosocial Characteristics of Pediatric Transplantation Candidates–Evaluation Scale (PPCPT-ES)

The PPCPT-ES consists of 18 items created by child and adolescent psychiatry specialists. Items are scored on a 10-point scale (0 = not at all, 10 = very much). The last four items are reverse-scored.

Schedule for Affective Disorders and Schizophrenia for School-Age Children – Present and Lifetime Version (K-SADS-PL-T, Turkish DSM-5 Version)

This semi-structured interview schedule was updated by Kaufman et al. according to DSM-5 diagnostic criteria [32]. The Turkish version was adapted by Ünal et al. The first section includes an unstructured interview and questions about sociodemographic characteristics, presenting complaints, developmental history, and general functioning. The second section covers over 200 specific symptoms within the past two months and across the lifetime. The third section consists of diagnostic assessments designed to confirm DSM-5 diagnoses. Information from multiple sources is evaluated separately and then integrated with the clinician's observation notes [33].

Following all these assessments, psychiatric diagnoses and treatment plans were established in accordance with DSM-5 criteria, under the supervision of a faculty member. Patients' suitability for transplantation was also evaluated [34].

Statistical Evaluation

As part of the PPCPT-ES development study, reliability analyses were conducted to evaluate the psychometric properties of the data collected from the sample group. Interrater reliability analyses of the scale items, based on evaluations by two independent expert raters, were performed first. Since each scale item had a continuous variable structure, the intraclass correlation coefficient (ICC) was calculated. This allowed for the determination of both absolute agreement between raters for individual items and absolute agreement across the entire scale. Absolute agreement indicates that different raters assign the same or highly similar scores to the same subject.

In addition, further psychometric examinations were conducted, including exploratory factor analysis, comparisons of total scale scores with selected demographic variables, and descriptive statistics of the sample group.

All statistical analyses were performed using IBM SPSS Statistics for Windows, Version 22.0 (IBM Corp., Armonk, NY, USA). For comparisons of mean total scores obtained from participants, parametric tests such as two-way analysis of variance (ANOVA), independent samples t-test, and Pearson correlation coefficient were used under the assumptions of normal distribution and homogeneity of variances. When these assumptions were not met, non-parametric statistical methods were applied.

Results

Sociodemographic and Clinical Characteristics

The study included 34 transplant candidates: 10 kidney, 7 liver, 16 heart, and 1 lung transplant candidates. Among them, 21 were female (61.8%) and 13 were male (38.2%). Participants were distributed across age groups: 23.5% were in the preschool period, 29.4% (n=10) were aged 6–11, and 47.1% (n=16) were aged 12–18. Approximately half of the parents had completed only primary education (mothers 61.7%, fathers 44.1%). A lifetime psychiatric history was reported in 41.7% of patients, and 32.4% were actively experiencing psychiatric problems.

One-quarter of the families (n=8) were economically disadvantaged. About half of the patients (n=14) lived in a different city than the transplant center and relied either on another person's vehicle (17.6%) or on public transportation (29.4%) to access care. The majority of patients (79.4%) were informed about the transplantation process, while the preschool group and patients in intensive care (20.6%) were not. Among those informed, the information was predominantly provided by organ transplant nurses (88.8%) (Table 1 and Table 2).

Reliability Analysis

Inter-Rater Consistency

The inter-rater reliability of PPCPT-ES scores was evaluated using the ICC method with ratings from two expert assessors. Intra-class correlation values were initially calculated separately for each of the 18 items. Reliability coefficients, based on the two-way random effects model, indicated statistically significant agreement between raters for all 18 items. Average consistency values ranged from 0.41 to 0.94 for intraclass correlation and from 0.26 to 0.88 for single measurements. Cronbach's alpha values were also within this range.

According to established criteria, intraclass correlation values are classified as poor when $r < 0.40$, moderate when $r = 0.40–0.59$, good when $r = 0.60–0.74$, and excellent when $r > 0.75$ [35]. Based on the total PPCPT-ES scores, the ICC was 0.97 for the average measurement and 0.88 for the single measurement. However, item 12 yielded an insignificant F value (Table 3).

Table 1. Sociodemographic and Clinical Characteristics

Feature	Variable	n	%
Gender			
	Female	21	61,8
	Male	13	38,2
Age			
	0-5	8	23,5
	6-11	10	29,4
	12-18	16	47,1
Mother's Education Level			
	Primary education	21	61,7
	High school	4	11,7
	University	9	26,4
Father's education Level			
	Primary education	15	44,1
	High school	11	32,3
	University	8	22,8
Number of Children to be Cared for by the Mother			
	1	8	23,5
	2	14	41,2
	3	6	17,6
	4+	6	17,7
Economic Inefficiency			
	Yes	8	23,5
	No	24	70,6
Active Psychiatric Illness			
	Yes	11	32,4
	No	23	67,6
Lifetime Psychiatric Illness			
	Yes	14	41,7
	No	20	58,8
Location of the Family in relation to the Transplant Center			
	Urban	14	41,2
	Rural	20	58,8
Transportation to the Treatment Center			
	Own vehicle	18	52,9
	Other's vehicle	6	17,6
	Public transfer	10	29,4

Table 2. Sociodemographic and Clinical Characteristics

	n	%
Planned Organ Transplant		
Kidney	10	29,4
Liver	7	20,6
Heart	16	47,1
Lung	1	2,9
Organ Donor Type		
Live	11	36,7
Cadaver	19	63,3
Additional Chronic Disease		
Yes	8	23,5
No	26	76,5
Patient's Knowledge about the Transplantation Process before Consultation		
Yes	27	79,4
No	7	20,6
Information Source on the Transfer Process		
Organ Transplant Nurse	24	88,8
Internet	2	7,4
Physician	1	3,7
Risk Factors to Disrupt Adaptation to the Transplant Process		
Multiple Complex Drug Use	2	8,6
Active Psychiatric Illness	11	47,8
Cost of Treatment	1	4,3
Difficulty in Access to Treatment Center	3	13,0
İntellectual Disability	6	26,0

Internal Consistency

Item-total correlations and internal consistency reliability analyses were performed separately for both raters across the 18 PPCPT-ES items. Although Cronbach's alpha coefficients for both raters were adequate, the item-total correlations for items 4 (the family's motivation for transplantation), 7 (the patient's current substance use), 12 (the family's cooperation with the treatment team), and 14 (the patient's cooperation with the school) were below 0.20. Furthermore, item 12 was insignificant in inter-rater consistency analysis. These four items were therefore excluded.

For the remaining 14 items, item-total correlations ranged from 0.29 to 0.72 for rater 1 and from 0.25 to 0.70 for rater 2. Cronbach's alpha for both raters was 0.86, indicating high internal consistency. These findings suggest that the PPCPT-ES measures a homogeneous construct as a continuous variable and can be reliably applied (Table 4).

To further examine agreement, an independent samples t-test was conducted on the mean scores of the two raters across the 14 retained items. No statistically significant difference was observed ($t = -0.264$, $df = 64$, $p = 0.792$). This confirms that the two raters provided consistent evaluations, supporting the homogeneity of the scale.

Correlation Analysis

Pearson correlations were calculated between PPCPT-ES total scores and scores from the Hope in Children Scale and the Satisfaction with Life Scale for Children. Total scores

Table 3. Inter-rater intraclass correlation consistency values of psychiatric and psychosocial characteristics of pediatric transplantation candidates-evaluation scale (PPCPT-ES)

Item No	Cronbach Alpha	Intraclass Correlation Single measurement	Intraclass Correlation Averaging measurement	F	Sd_1	Sd_2
1	.939	.883	.938	16.160***	32	32
2	.715	.556	.715	3.504***	32	32
3	.923	.857	.923	12.948***	32	32
4	.515	.347	.515	2.063 *	32	32
5	.814	.687	.814	5.383***	32	32
6	.847	.734	.847	6.518***	32	32
7	.730	.575	.730	3.706***	32	32
8	.831	.711	.831	5.913***	32	32
9	.820	.694	.820	5.547***	32	32
10	.790	.653	.790	4.758***	32	32
11	.902	.822	.902	10.236***	32	32
12	.415	.262	.415	1.708 a.d	32	32
13	.513	.345	.513	2.055*	32	32
14	.866	.763	.866	7.457***	32	32
15	.796	.660	.796	4.890***	32	32
16	.812	.683	.812	5.308***	32	32
17	.815	.688	.815	5.416***	32	32
18	.790	.653	.790	4.757***	31	31
Total	.89	.80	.89	8.959***	32	32

P***<.001; p*<,05; a.d= not significant.

from both raters were derived for the 14 retained items.

Results indicated a positive, moderate correlation between transplantation suitability scores from rater 2 and hope scores ($r = 0.58$, $p < 0.01$). Hope scores also showed a strong, positive correlation with life satisfaction ($r = 0.72$, $p < 0.001$). Moreover, a strong correlation was found between the suitability scores of rater 1 and rater 2 ($r = 0.80$, $p < 0.001$). These findings suggest that higher transplantation suitability is associated with greater hope, which in turn is linked to higher life satisfaction (Table 5).

Differences by Age Group and Transplant Type

A two-way ANOVA (2 × 3 design) was conducted to examine differences in PPCPT-ES total scores by age group (0–11 years vs. 12–18 years) and transplant type (kidney, liver, heart). PPCPT-ES scores were averaged across the two raters.

Results revealed a significant interaction effect between age and transplant type ($F(2,32) = 14.386$, $p < 0.001$, $\eta^2 = 0.525$). A significant main effect was also found for transplant type ($F(2,32) = 6.894$, $p < 0.001$, $\eta^2 = 0.347$), whereas the main effect of age was not significant ($F(1,32) = 3.491$, $p > 0.05$, $\eta^2 = 0.118$). Although post-hoc comparisons did not reveal significant pairwise differences, the interaction effect explained 52% of the variance.

Mean PPCPT-ES scores were as follows:

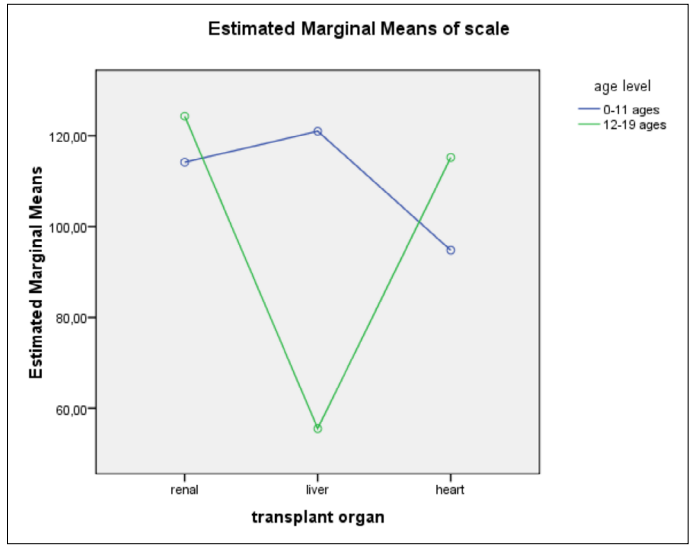

Fig. 1. Mean PPCPT-ES total scores by age group (0–11 years, 12–18 years) and type of transplantation (kidney, liver, heart).

Kidney transplantation: 114.17 (SD = 5.45) for ages 0–11; 124.33 (SD = 7.71) for ages 12–18.

Liver transplantation: 121.00 (SD = 5.45) for ages 0–11; 55.00 (SD = 13.35) for ages 12–18

Heart transplantation: 94.00 (SD = 5.97) for ages 0–11; 115.23 (SD = 4.03) for ages 12–18 (Fig. 1).

In summary, significant differences in psychiatric suitability

Table 4. Internal consistency reliability analysis values of psychiatric and psychosocial characteristics of pediatric transplantation candidates-evaluation scale (PPCPT-ES)

ITEMS	1st rater			2nd rater		
	Avg. N=33	S N=33	Item Total Score cor. N=33	Avg. N=32	S N=32	Item Total Score cor. N=32
1. Patient's level of knowledge about the transplant process	5.91	3.59	.58	6.06	3.57	.61
2. The level of knowledge of the patient's family about the transplantation process	7.85	2.05	.39	7.97	1.84	.42
3. Patient's willingness/motivation level for organ transplantation	7.12	3.39	.56	7.31	2.96	.67
4. Patient's level of communication with the treatment team	7.85	2.61	.69	7.72	2.40	.62
5. Patient's level of cooperation with the treatment team	8.39	2.16	.58	8.34	2.30	.69
6. The level of economic and logistical support needed by the patient's family	7.94	1.80	.26	7.12	2.21	.46
7. The level of support of the patient by close family members	8.48	1.68	.29	7.84	2.06	.64
8. Social support level of the patient	7.73	2.07	.66	7.94	1.92	.67
9. Patient's level of trust in the transplant and surgical team	8.21	2.47	.49	8.00	2.44	.26
10. The level of trust of the patient's family in the transplant and surgical team	8.94	1.01	.29	8.78	1.29	.25
11. The level of risk factors that may impair the patient's current compliance with treatment	8.09	2.55	.72	7.88	2.69	.49
12. The level of negative impact of the patient's current psychiatric symptoms on transplantation	8.85	2.00	.69	8.59	1.81	.60
13. Risk level of family conflict with the treatment team in case of a possible complication after transplantation	8.12	1.95	.64	8.53	1.87	.70
14. Level of conflict between caregivers/parents	8.73	1.42	.41	8.84	1.94	.29
Cronbach's Alpha for the whole test		0.86			0.86	

Table 5. Correlation, average and standard deviation values between psychiatric and psychosocial characteristics of pediatric transplantation candidates-evaluation scale (PPCPT-ES) total scores and hope and life satisfaction scales

	Ort. (S)	Median	Skewness value	Kurtosis value	Shapiro Wilk	1.	2.	3.	4.
1.Evaluation-1 Total score	112.2 (19.1)	116	-1,21	1,29	,005	1.00	.80***	.36	.15
2. Evaluation-2 Total score	110.9 (19.4)	115	-1,19	1,35	0,010		1.00	.58**	.30
3. Hope scale Total score	25.3 (6.2)	27	-,524	-,231	,169			1.00	.72***
4. Life satisfaction scale Total score	16.4 (5.4)	16	-0071	-,909	,250				1.00

P***<.001; p**<.01; 1: Assessment-1 Total score; 2: Assessment-2 Total score; 3: Hope scale total score; 4: Life satisfaction scale total score.

for transplantation were observed across transplant types and age groups, with a particularly strong interaction effect, highlighting the importance of considering both variables simultaneously when evaluating candidates.

Discussion

In this study, a comprehensive measurement tool was developed to standardize the psychosocial assessment process for transplant candidates, reduce prejudice, and identify the common strengths and weaknesses of patients and their families that may influence post-transplant treatment outcomes.

Non-adherence to immunosuppressive treatment is one of the most important causes of long-term mortality after organ transplantation [36]. Standardized pre-evaluation and follow-up enable early interventions before non-adherence occurs. Moreover, the development of organ-specific and culturally appropriate scales would enhance

the identification of at-risk pediatric patients. Key factors assessed include the child's and family's understanding of the transplantation process, psychiatric status, compliance with medical treatment and immunosuppressive therapies, readiness to assume post-transplant responsibilities, cognitive performance, family financial resources, and coping mechanisms. If a psychiatric history exists, the risk of exacerbation or relapse should also be considered. The pharmacokinetics and pharmacodynamics of psychotropic drugs in the context of organ failure must be evaluated when planning treatment. In addition to the psychiatric side effects of immunosuppressive therapy, possible post-transplant psychiatric disorders should be identified and managed. The use of psychotropic drugs in the post-transplant period requires careful attention to drug interactions [22].

A study conducted in Türkiye with 59 pediatric transplant patients between 2012 and 2015 found high rates of psychiatric disorders before transplantation, ranging from 60% to 69.4% among heart, kidney, and liver transplant candidates [37]. In our study, active psychiatric illness was observed in 32.4% of patients, and 41.7% reported a lifetime history of psychiatric illness.

Family dynamics and caregiver coping styles have also been shown to influence transplant outcomes. One study of pediatric heart transplant patients found that family functioning in the first two years post-transplant was significantly related to treatment adherence [38]. Another study investigating coping strategies in caregivers of adolescent heart transplant (HTx) recipients and HTx candidates using left ventricular assist devices (LVAD) reported that optimistic and confident coping strategies were associated with fewer internalizing symptoms and higher quality of life in adolescents [39]. Consistently, our findings showed that higher suitability for transplantation was associated with increased levels of hope, which in turn contributed to greater life satisfaction.

Strong risk factors for non-adherence after kidney transplantation include prior history of non-adherence and adolescence or young adulthood. Additional risk factors with consistent but smaller effects include minority race/ethnicity, poor social support, and poor perceived health. In pediatric patients, parental distress and psychological functioning also play a crucial role [40]. Low socioeconomic status has been independently associated with poor graft outcomes in pediatric kidney transplantation [41].

Several scales have been developed to systematize psychosocial assessment prior to solid organ transplantation in adults. These include the Edmonton Symptom Rating System, Stanford Integrated Psychosocial Assessment of Transplantation (SIPAT), Structured Interview for Kidney Transplantation (SIRT), Transplant Evaluation Rating Scale (TERS), Psychosocial Assessment of Transplantation Candidates (PACT), and INTERMED. For pediatric patients, the Stanford Pediatric Psychosocial Transplantation Tool is under development. To date, the Pediatric Transplant Rating Instrument (P-TRI) remains the only validated tool for psychosocial assessment in pediatric transplantation [19]. The Turkish version of the P-TRI has shown good psychometric validity in pediatric kidney transplant recipients, distinguishing between "risky" and "risk-free" candidates in pre-transplant assessment [36].

The PPCPT-ES, developed in this study, is a 14-item semi-structured interview tool designed to assess psychosocial risk domains in pediatric transplant candidates. Information was obtained through direct interviews with candidates and families, supplemented by medical records and input from the transplant team. Items were derived from a review of the literature on pediatric psychosocial risk factors, particularly those linked to treatment adherence. The scale was intended to support the standardized identification of psychosocial vulnerabilities that could compromise post-transplant outcomes.

Unlike adult-oriented instruments, our scale incorporates a developmental perspective for children with chronic illness and emphasizes family-related factors that influence outcomes. Importantly, the PPCPT-ES does not employ cut-off scores to predict clinical outcomes. Instead, it highlights specific areas of concern that can be addressed with pre- or post-transplant interventions. By systematically identifying psychosocial vulnerabilities, the tool provides the transplant team with comprehensive insights into potential barriers to adherence and supports the design of targeted psychosocial interventions. Although numerous studies have explored associations between psychosocial risk factors and treatment outcomes, clear causal links between psychosocial characteristics and graft survival remain limited [19]. Consequently, no weighting system was applied to individual subscales or items.

Correlation analyses further demonstrated that higher transplantation suitability scores were positively associated with greater hope, and that higher levels of hope correlated with greater life satisfaction. Taken together, these results indicate that psychosocial suitability for transplantation

may contribute to improved well-being and quality of life in pediatric patients. The high internal consistency reliability of the PPCPT-ES (Cronbach's alpha = 0.86) underscores the tool's robustness as a standardized measure.

Overall, this study provides promising evidence for the use of PPCPT-ES in identifying psychosocial vulnerabilities and predicting treatment compliance in pediatric organ transplant candidates.

Limitations

This study has several limitations. First, all patients in the sample were deemed eligible for transplantation. Therefore, the study could only assess post-transplant outcomes in relation to overall lower scale scores, limiting generalizability. Second, the absence of scale scores specific to each transplant organ group is another restriction. Third, the study lacked post-transplant follow-up data. To address this, we plan to continue monitoring the sample and collect data at 3, 5, and 10 years to further evaluate the utility of the tool.

Finally, the scale was administered by only two observers. While this is not a major limitation, it should be noted that the inclusion of more raters could further enhance the accuracy of inter-rater reliability assessments.

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EUROPEAN TRANSPLANT RESEARCH

CASE REPORT

Intracamaral recombinant tissue plasminogen activator as a treatment for refractory fibrin reaction following penetrating keratoplasty: A case report

Beyzanur Karaca, Özlem Dikmetaş, Sibel Kocabeyoğlu

Department of Ophthalmology, Hacettepe University Ankara, Turkiye

Abstract

We report a case of severe fibrin reaction following penetrating keratoplasty (PKP) that was successfully treated with intracameral recombinant tissue plasminogen activator (r-TPA). A 62-year-old male with a history of herpetic keratitis and retinal detachment surgery presented with corneal scarring in the left eye. He underwent PKP combined with cataract extraction and intraocular lens (IOL) implantation. One month postoperatively, he developed an intense anterior chamber reaction with fibrin accumulation, endothelial plaque formation on the graft, and creamy-white iris infiltrates, raising suspicion of fungal keratitis. Therapeutic PKP was performed due to treatment-resistant ulcerative keratitis, and the patient subsequently received an intracameral injection of r-TPA (25 µg/0.05 cc) for persistent fibrinoid reaction. At the 24-hour follow-up, the fibrin had markedly resolved, and the graft appeared clear. While topical or subconjunctival steroids may be sufficient in mild to moderate cases, intracameral r-TPA may serve as a valuable adjunct in refractory cases, offering long-term morphological and functional improvement.

Keywords: r-TPA, keratitis, penetrating keratoplasty, case report

Fungal keratitis is a significant cause of corneal blindness worldwide, particularly in developing regions where agricultural trauma is common [1]. It represents a severe form of infectious keratitis caused by fungal invasion of the corneal tissue, most frequently by filamentous fungi such as Fusarium and Aspergillus, or yeasts such as Candida [2]. Clinically, it presents with corneal ulceration, stromal infiltration, endothelial plaques, hypopyon, or fungal balls in the anterior chamber [2,3].

Management of fungal keratitis is challenging due to delayed diagnosis, limited antifungal options, and poor ocular drug penetration. Topical antifungal agents often demonstrate suboptimal bioavailability, and treatment responses are frequently incomplete [2]. Even natamycin 5%, the most widely used agent for filamentous fungal infections, has poor stromal penetration in deep infections [4]. Consequently, surgical interventions such as therapeutic or tectonic penetrating keratoplasty (PKP) are often required to eradicate infection or restore ocular integrity [5,6].

Severe intraocular inflammation associated with fungal keratitis can result in dense fibrinous anterior chamber

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Correspondence: Beyzanur Karaca, M.D. Department of Ophthalmology, Hacettepe University Ankara, Turkiye
E-mail: beyzanurkaraca97@gmail.com

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reactions. These membranes impair fundus visualization, complicate further surgical intervention, and may lead to sequelae such as posterior synechiae or angle-closure glaucoma [7]. While topical corticosteroids are widely used to suppress inflammation, their role in fungal keratitis is limited due to the risk of exacerbating microbial proliferation [3,7].

Recombinant tissue plasminogen activator (r-TPA) is a fibrin-specific fibrinolytic agent that catalyzes plasminogen-to-plasmin conversion, facilitating clot breakdown. Intracameral r-TPA has been reported as an effective adjunctive therapy for severe anterior chamber fibrin in various clinical contexts, including postoperative inflammation and endophthalmitis [8–10]. In eyes unresponsive to conventional anti-inflammatory therapies, r-TPA may promote anterior chamber clearing and support visual rehabilitation [10].

Case Report

A 62-year-old male presented with corneal opacity in the left eye. His history included penetrating keratoplasty (PKP) for herpetic keratitis and retinal detachment surgery due to high myopia two decades earlier. His medical history was otherwise unremarkable except for type 2 diabetes mellitus.

Best-corrected visual acuity (BCVA) was 20/20 in the right eye and hand motion in the left eye. Slit-lamp examination revealed a normal anterior segment in the right eye, while the left eye showed a +4 anterior chamber reaction, raising suspicion of graft rejection. Intraocular pressure (IOP) was 15 mmHg in the right eye and 14 mmHg in the left eye. The patient was bilaterally phakic. Fundus examination was normal in the right eye but obscured in the left eye; B-scan ultrasonography revealed no signs of intraocular inflammation or retinal detachment.

Topical dexamethasone was increased to hourly dosing, and a subconjunctival dexamethasone injection (0.4 mg/0.1 mL) was given. Three days later, the left eye developed intense flare and fibrin accumulation, endothelial plaque on the graft, and round creamy-white iris infiltrates. The conjunctiva was hyperemic with marked ciliary injection. BCVA declined to light perception. Fungal keratitis was suspected, and treatment with topical 0.3% fluconazole, amphotericin B, cefazolin, and gentamicin was initiated. Based on infectious disease consultation, intravenous and topical 1% voriconazole were added. Aqueous humor sampling, intrastromal, and intracameral voriconazole injections (50 µg/0.1 mL) were performed. Microbiological cultures showed no growth.

Highlights

- Severe fibrin reaction after penetrating keratoplasty can complicate fungal keratitis management and threaten graft survival
- Intracameral r-TPA provided rapid and effective fibrin resolution when conventional therapy failed
- r-TPA may serve as a valuable adjunct in refractory anterior chamber fibrin cases following therapeutic keratoplasty

After one week, IOP rose to 27 mmHg with ocular pain, leading to graft edema. Systemic acetazolamide was added. The anterior chamber fibrinoid reaction persisted with no regression of iris or graft infiltrates (Fig. 1A).

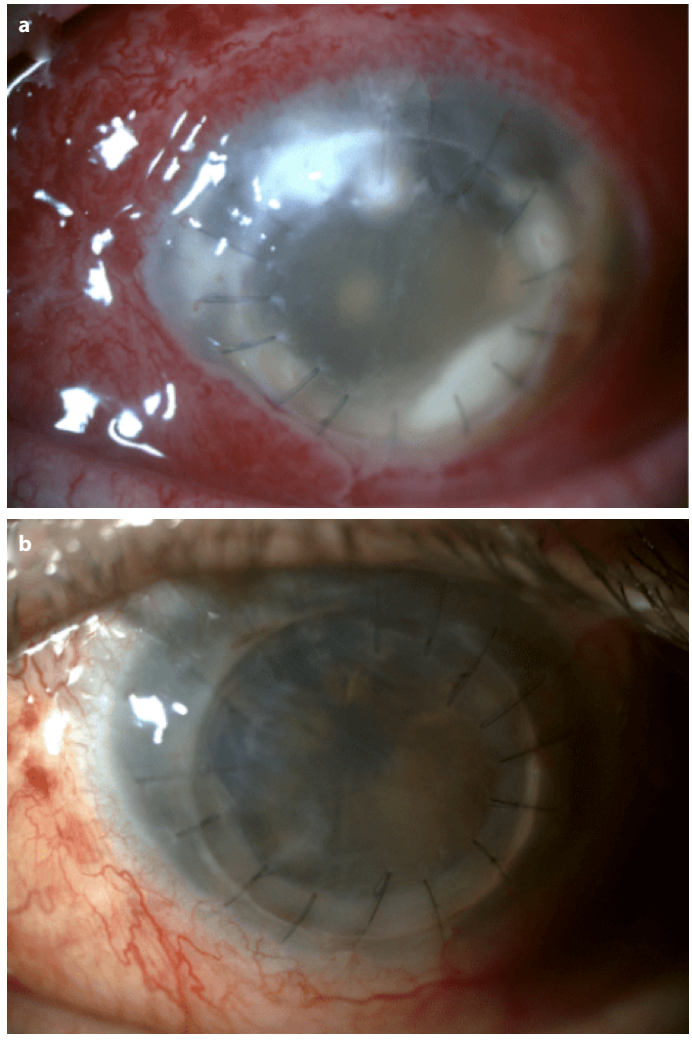

Fig. 1. Postoperative anterior segment findings. **(a)** Slit-lamp image showing intense anterior chamber fibrinoid reaction, endothelial plaque formation on the corneal graft, and round creamy-white infiltrates on the iris suggestive of fungal infection. The conjunctiva is markedly hyperemic with significant ciliary injection. **(b)** Following repeat penetrating keratoplasty and intensified antifungal therapy, the corneal graft appears clearer with residual posterior synechiae and persistent anterior chamber fibrinoid reaction.

The patient underwent repeat PKP (re-PKP) with anterior chamber lavage. Intraoperatively, a fibrinoid membrane and posterior synechiae were noted. Histopathology of the excised graft confirmed fungal hyphae and spores; Candida albicans was isolated from aqueous humor. Postoperatively, systemic therapy was adjusted to oral voriconazole. Topical antifungals were tapered only after complete clinical resolution and maintained for 12 weeks at a low dose.

By postoperative day 3, active infection had subsided. However, dense posterior synechiae developed, and the fibrinoid anterior chamber reaction persisted (Fig. 1B). IOP measured 25 mmHg. The patient was treated with intracameral r-TPA (25 µg/0.05 cc).

At 24 hours, fibrin had significantly resolved and the graft appeared clear (Fig. 2). IOP was 18 mmHg. No complications such as hypotony, corneal edema, or anterior segment toxicity were observed. Two weeks later, persistent posterior synechiae necessitated pupilloplasty. Postoperatively, the graft remained clear and BCVA improved to hand motion.

This represents one of the few reported cases in which intracameral r-TPA was successfully used for persistent anterior chamber fibrin following fungal keratitis treated with therapeutic PKP.

Discussion

Fungal keratitis is often complicated by severe intraocular inflammation, leading to fibrin deposition in the anterior chamber. This process arises from blood-aqueous barrier disruption and fibrinogen accumulation, particularly when corticosteroids are restricted to avoid exacerbating infection [1,4]. Persistent fibrin membranes can result in posterior synechiae, pupillary block, secondary glaucoma, and reduced intraocular drug penetration [5,9]. Despite maximal antifungal therapy, many patients ultimately require PKP [5,6]. In our case, fibrin formation persisted postoperatively, necessitating additional intervention.

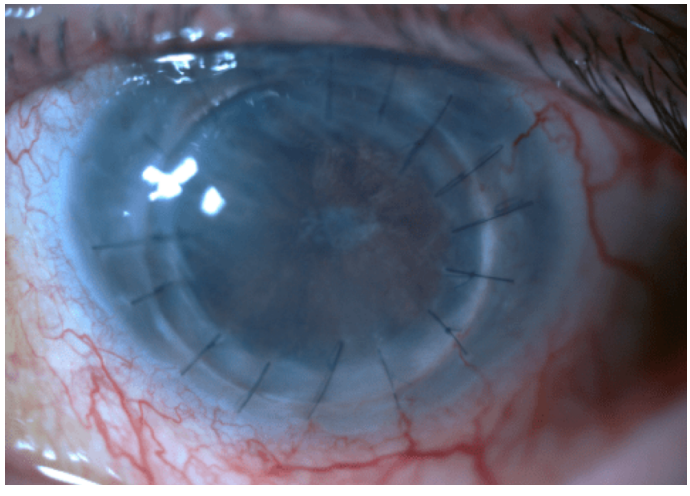

Fig. 2. Postoperative anterior segment findings after intracameral recombinant tissue plasminogen activator (r-TPA) injection. The corneal graft appears clearer with reduced fibrinoid reaction and improved visibility of the anterior chamber structures.

Recombinant tissue plasminogen activator (r-TPA) is a fibrin-specific serine protease that induces localized fibrinolysis via plasminogen activation. At low intracameral doses (5–25 µg), it rapidly dissolves fibrin without significant ocular toxicity [9,10]. In this case, r-TPA enabled complete fibrin resolution, restored pupillary visualization, and facilitated postoperative monitoring. This outcome aligns with prior reports describing rapid fibrinolysis after r-TPA in postoperative inflammation and endophthalmitis [9,10]. Although evidence remains limited in fungal keratitis, our case highlights its potential role in this setting.

Previous reports have described the use of r-TPA in microbial keratitis-related anterior chamber fibrin. Riaz et al. demonstrated clearance within two hours in postoperative endophthalmitis [10], and Sherman reported its intraoperative application during keratoplasty for infectious keratitis to prevent pupillary block [11]. Together with our findings, these observations suggest that r-TPA may be considered for selected fungal keratitis cases complicated by dense, refractory fibrin, provided infection control is achieved.

In conclusion, intracameral r-TPA may serve as an effective adjunct to surgical and antifungal management of fungal keratitis complicated by severe fibrin reaction. By addressing the inflammatory by-products of infection, r-TPA may reduce complications and improve visual outcomes. Although our results were favorable, clinicians should remain cautious of potential adverse effects such as transient hypotony, corneal edema, or endothelial toxicity, which have been reported in rare cases [9,10]. This case contributes practical insight into the potential role of fibrinolytic therapy in a surgically managed, steroid-limited context of infectious keratitis.

Informed Consent: Written informed consent was obtained from the patient for the preparation of this work.

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EUROPEAN TRANSPLANT RESEARCH

CASE REPORT

Corneal transplant in topical anesthetic abuse keratopathy: To do or not to do?

İlayda Korkmaz,[1] Melis Palamar,[2] Sait Eğrilmez,[2] Ayşe Yağcı[2]

[1]Department of Ophthalmology, Bandirma Training and Research Hospital, Balikesir, Turkiye
[2]Department of Ophthalmology, Ege University, Izmir, Turkiye

Abstract

This study reports the outcomes of corneal transplantation in two cases of topical anesthetic abuse keratopathy. A chart review was performed for two patients who underwent penetrating topical anesthetic abuse keratoplasty (PK) due to keratopathy-related sequelae. The first case presented with unilateral full-thickness corneal perforation and a best-corrected visual acuity (BCVA) of hand motion. A tectonic PK was performed to restore globe integrity; however, the patient continued using topical anesthetic drops, and eight months postoperatively developed graft failure, with a final BCVA of hand motion. The second case presented with a unilateral corneal scar due to topical anesthetic abuse, with an initial BCVA of hand motion. PK was performed for visual rehabilitation, and the early postoperative course was uneventful with BCVA of 20/50. The patient missed scheduled follow-up visits and returned at the third postoperative month with loose sutures and signs of graft rejection. After suture removal and topical therapy, the clinical findings improved, and the final BCVA was 20/100. Psychiatric evaluation of both patients revealed severe anxiety and aggression. These cases highlight that uncontrolled use of topical anesthetic eye drops leads to irreversible ocular surface damage, and corneal transplantation in such patients has limited success due to poor compliance, often resulting in graft rejection and graft failure.

Keywords: Corneal transplant, graft failure, topical anesthetic abuse keratopathy

Topical anesthetic abuse is one of the leading causes of toxic keratopathy with serious visual consequences. It may cause a wide spectrum of ocular surface problems, ranging from punctate keratopathy to corneal perforation. The frequency, dose, and duration of topical anesthetic use, individual susceptibility, and the specific anesthetic agent determine the severity of ocular damage [1–3]. This self-inflicted keratopathy is relatively rare in countries where such medications are not available over the counter. However, in regions where access is easy, its incidence is higher. Clinically, this entity can mimic infectious keratitis, particularly Acanthamoeba keratitis, which complicates diagnosis [4]. As a result, diagnosis is often delayed, and patients' poor compliance with treatment further worsens the visual prognosis [1]. Persistent epithelial defects, corneal scarring, progressive stromal melting, and corneal perforations are among the most important causes of vision loss in topical anesthetic abuse keratopathy. Although both medical and surgical treatments may help stabilize the ocular surface and prevent further complications, the

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Correspondence: İlayda Korkmaz, M.D. Department of Ophthalmology, Bandirma Training and Research Hospital, Balikesir, Turkiye
E-mail: ilaydaakorkmazz@gmail.com
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overall anatomical and visual prognosis is usually poor due to patient noncompliance [3,5].

The purpose of this report is to present the outcomes of corneal transplantation in patients with topical anesthetic abuse keratopathy.

Case 1

A 34-year-old female presented to the emergency department with complaints of redness, pain, and vision loss in the left eye for one week. There was no history of ocular trauma, surgery, or contact lens use. Her medical history revealed that she had been diagnosed with corneal epithelial abrasion in the left eye and had been prescribed topical antibiotics (0.3% netilmicin, Netira, SIFI, Italy) and preservative-free artificial tears (0.15% sodium hyaluronate, Eyestil SD, SIFI, Italy) six weeks earlier. Since then, she had been using topical anesthetic drops (0.5% proparacaine hydrochloride, Alcaine, Alcon, USA), available over the counter, to relieve ocular pain.

At presentation, best-corrected visual acuity (BCVA) was 20/20 in the right eye and hand motion in the left. Anterior and posterior segment examinations were unremarkable, and intraocular pressure (IOP) was within normal limits in the right eye. Slit-lamp examination of the left eye revealed a full-thickness corneal perforation with a dense, well-circumscribed stromal ring infiltrate and surrounding stromal edema. The infiltrate appeared whitish, sharply demarcated, and involved the mid-peripheral cornea. The Seidel test was positive, the anterior chamber was shallow, and IOP was low.

The patient was hospitalized, and anesthetic eye drops were discontinued immediately. Although the ring-shaped infiltrate initially raised suspicion for infectious keratitis, the patient's history of unsupervised topical anesthetic use and neurotrophic epitheliopathy supported a diagnosis of topical anesthetic abuse keratopathy. Corneal microbiological examination revealed no infectious agents, confirming the non-infectious etiology. Psychiatric evaluation revealed severe anxiety and aggression, and she was prescribed diazepam 10 mg orally twice daily (Nervium, Saba, Istanbul, Türkiye) and indomethacin 50 mg orally twice daily (Endol, Deva, Türkiye). Conservative treatment was initiated with topical antibiotics (0.5% moxifloxacin, Moxai, Abdi İbrahim, Türkiye), preservative-free artificial tears (0.15% sodium hyaluronate, Eyestil SD, SIFI, Italy), systemic doxycycline (200 mg/day, Tetradox, Teva Pharmaceuticals, Türkiye), and bandage contact lenses.

Highlights

- Unsupervised use of topical anesthetic eye drops can lead to severe keratopathy, permanent vision loss, and poor graft survival after corneal transplantation
- Corneal transplantation in patients with anesthetic abuse keratopathy shows limited success due to continued drug use and poor compliance with follow-up
- Psychiatric consultation and strict regulation of over-the-counter anesthetic availability are essential for prevention and better clinical outcomes

After five days without significant improvement, tectonic penetrating keratoplasty (PK) was performed due to corneal perforation secondary to anesthetic abuse. During keratoplasty, 7.5–7.75 mm vacuum-punch trephines were used, and the donor button was sutured with interrupted 10-0 nylon. No intraoperative complications occurred. Postoperatively, she received topical corticosteroids (0.1% dexamethasone, Maxidex, Novartis, Switzerland), antibiotics (0.5% moxifloxacin), cyclosporin (0.05% cyclosporin A, Depores, Deva, Türkiye), and preservative-free artificial tears. Early postoperative follow-up was uneventful, with a clear graft and intact epithelium.

Eight months later, she presented with redness, pain, and blurred vision in the left eye. BCVA was hand motion, and slit-lamp examination revealed graft failure with edema and neovascularization. Anamnesis revealed continued topical anesthetic use and poor compliance with prescribed treatment. She declined repeat PK, and her condition remained stable over eight years of follow-up with a final BCVA of hand motion. Written informed consent was obtained.

Case 2

A 38-year-old male presented with photophobia and vision loss in the left eye for three months. He had a history of multiple visits to ophthalmology clinics with persistent epithelial defect and reported prior exposure to arc welding flash. Following this, he began using topical anesthetic eye drops (0.5% proparacaine hydrochloride, Alcaine, Alcon, USA), obtained over the counter.

At presentation, BCVA was 20/20 in the right eye and hand motion in the left. Anterior and posterior segment examinations were unremarkable, and IOP was within normal limits in the right eye. Slit-lamp evaluation of the left eye revealed corneal neovascularization and a dense stromal opacity involving the visual axis (Fig. 1). Fundus visualization was not possible, though ultrasonography and IOP were normal.

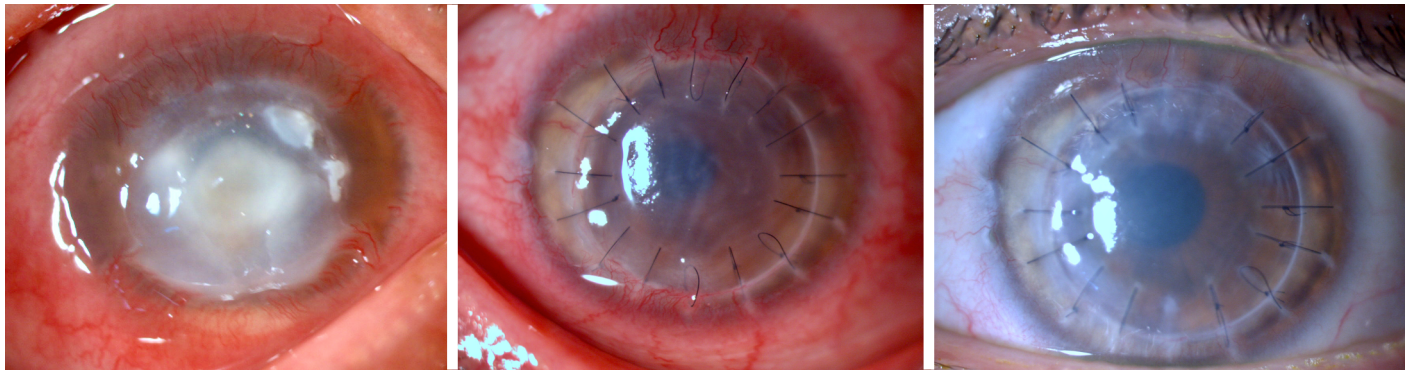

Fig. 1. Anterior segment photograph of Case 2 showing preoperative corneal neovascularization, ring-shaped infiltration, and dense stromal opacity involving the visual axis; three months after penetrating keratoplasty, loose sutures and graft edema are evident, with subsequent improvement following suture removal.

The patient was counseled about the harmful effects of anesthetic eye drops and the importance of discontinuation. Psychiatric evaluation revealed symptoms of anxiety and aggression, and he was prescribed diazepam 10 mg orally twice daily and indomethacin 50 mg orally twice daily. A PK was performed for visual rehabilitation due to corneal scarring from anesthetic abuse. No intraoperative complications occurred.

Postoperatively, he received topical corticosteroids (0.1% dexamethasone), antibiotics (0.5% moxifloxacin), cyclosporin (0.05% cyclosporin A), and preservative-free artificial tears. The early postoperative course was uneventful, with a BCVA of 20/50. However, the patient did not attend scheduled follow-up visits. Three months later, he presented with foreign-body sensation and blurred vision. Biomicroscopy revealed loose sutures, corneal edema, and keratic precipitates. BCVA was 20/400. The loose sutures were removed, and intensive topical corticosteroids and antibiotics were initiated with a diagnosis of allograft rejection. With treatment, the clinical picture improved, and the final BCVA was 20/100. Written informed consent was obtained.

Discussion

Regular instillation of topical anesthetics without medical supervision causes severe keratopathy by damaging the corneal microvilli and triggering cell death. Apart from its direct toxic effect on the epithelium, it disrupts normal corneal healing by damaging epithelial motility complexes [6–8]. Impaired corneal healing leads to persistent epithelial defects, corneal neovascularization, corneal scarring, and even blindness [1,9]. For this reason, it is not advisable to sell topical anesthetic drugs over the counter. These two cases occurred during the period when such agents were available without prescription in Türkiye. Fortunately, the Turkish Government prohibited the sale of these drugs in pharmacies on March 29, 2012, preventing further such consequences.

Early diagnosis and timely treatment are extremely challenging in topical anesthetic abuse keratopathy, as it can mimic infectious etiologies, especially Acanthamoeba keratitis. The presence of stromal inflammation resembling ring infiltration, severe pain disproportionate to clinical findings, and lack of response to broad-spectrum antibiotics complicate diagnosis [4]. Superinfection may also occur, as the damaged cornea is highly susceptible to secondary infections. Therefore, microbiological assessment of the affected cornea is valuable to exclude infectious keratitis [10,11]. In addition, physician awareness of the clinical features of anesthetic abuse keratopathy accelerates diagnosis. It is essential to include topical anesthetic abuse in the differential diagnosis and to take a detailed history along with clinical findings [1,5].

The outcome of topical anesthetic abuse cases is usually poor. Besides delayed diagnosis, patients' poor compliance with treatment also worsens long-term visual prognosis [1,2,5,12]. Rosenwasser et al. [1] reported poor final visual acuity in six patients with this condition. Informing patients and discontinuing anesthetic eye drops are the first and most critical management steps. However, motivating patients to adhere to treatment is often difficult, as they resist discontinuing the drug. Psychiatric consultation is highly recommended, since psychiatric disorders and other substance abuse frequently accompany these patients [12]. In our report, both patients exhibited severe anxiety and aggression, and were prescribed benzodiazepines and systemic analgesics to improve compliance.

The main goals of medical treatment are to promote re-epithelialization, stabilize the tear film, suppress ocular surface inflammation, and prevent devastating complications such as corneal perforation. First-line options include preservative-free artificial tears, autologous serum eye drops, topical anti-

inflammatory agents (cyclosporine and corticosteroids), systemic anti-collagenases (oral doxycycline), and prophylactic topical antibiotics to prevent secondary infections [3,10].

In persistent and progressive cases, surgical options such as amniotic membrane transplantation (AMT) have been reported to be beneficial [10,13]. Burcu et al. [13] emphasized the advantages of early AMT application in anesthetic abuse patients. However, despite these efforts, some patients develop serious sight-threatening complications such as stromal melting and corneal perforations, necessitating tectonic penetrating keratoplasty (PK). In many cases, the cornea heals with a dense stromal scar, resulting in permanent vision loss. Thus, PK is performed not only to restore anatomical integrity but also to provide visual rehabilitation [1,3,9].

The prognosis following PK in topical anesthetic abuse cases is generally poor. Continued anesthetic use in the postoperative period and poor compliance with follow-up contribute to graft rejection and failure. Furthermore, pre-existing ocular surface inflammation increases the risk of graft rejection and reduces graft survival [3,5,10]. Patients should be thoroughly informed of these risks, and postoperative follow-up should be carried out meticulously in close cooperation with the patient. Psychiatric support should also be included in the management.

Systemic analgesics are frequently needed in these cases due to the severe pain caused by discontinuation of the anesthetic. A multimodal approach targeting both nociceptive and neuropathic pain is often required. Nonsteroidal anti-inflammatory drugs (NSAIDs) or opioids may improve comfort and treatment adherence [14,15].

In conclusion, uncontrolled use of topical anesthetic eye drops results in permanent ocular surface damage. Even with close monitoring and intensive treatment, long-term prognosis is generally unfavorable. Early identification and treatment of patients at risk of anesthetic abuse are essential to prevent irreversible vision loss requiring corneal transplantation. Public awareness should be raised, and strict regulations should be enforced to prevent over-the-counter sales of topical anesthetics.

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EUROPEAN TRANSPLANT RESEARCH

REVIEW

Nursing approaches in immunosuppressive medication adherence

Büşra Selma Saha,[1] Yaprak Sarıgöl Ordin[2]

[1]Institute of Health Sciences, Dokuz Eylul University, Balçova/İnciraltı, Izmir, Turkiye
[2]Department of Surgical Nursing, Faculty of Nursing, Dokuz Eylul University, Balçova/İnciraltı, Izmir, Turkiye

Abstract

Organ transplant recipients must continue immunosuppressive therapy throughout their lives, and adherence to these medications is critical for long-term graft survival. Multiple factors influence adherence, including socioeconomic status, treatment-related variables, patient characteristics, disease-related factors, and components associated with the healthcare system and team. Addressing these multifactorial challenges requires the integration of educational, cognitive, behavioral, psychological, and emotional strategies. As integral members of the multidisciplinary healthcare team, nurses play a central role in identifying barriers to adherence, utilizing appropriate assessment tools, and implementing evidence-based, patient-centered interventions. This review highlights nurses' responsibilities and contributions in promoting adherence and supporting transplant recipients throughout their post-transplant journey.

Keywords: Immunosuppressive therapy, medication adherence, nursing care, organ transplantation, patient adherence.

In solid organ transplantation, immunosuppressive therapy is administered to suppress the immune response in the early post-transplant period, maintain long-term immune control, and prevent rejection. This therapy is critical not only for graft survival but also for the overall survival of the recipient. Oral administration is the most common route for long-term immunosuppressive therapy in transplant recipients. Although systemic administration routes (such as oral and intravenous) offer convenience, they may require high doses, carry a risk of adverse effects, and result in variability in drug efficacy. Due to their complex regimens and side-effect profiles, immunosuppressive medications are often associated with poor treatment adherence [1]. Non-adherence to an immunosuppressive regimen is one of the most significant challenges following organ transplantation.

Medication adherence is defined by the EMERGE (ESPACOMP Medication Adherence Reporting Guideline) framework as the process by which patients take their medications as prescribed, structured into three distinct phases: initiation (when the patient takes the first dose), implementation (the extent to which a patient's actual dosing corresponds to the prescribed regimen), and persistence (the time from initiation until the eventual discontinuation of therapy). This framework provides a standardized approach for measuring and reporting medication adherence in both research and clinical practice [2].

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Correspondence: Büşra Selma Saha. Institute of Health Sciences, Dokuz Eylul University, Balçova/İnciraltı, Izmir, Turkiye
E-mail: busraselmasaha@gmail.com
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Non-adherence to immunosuppressive therapy has been associated with severe complications across all types of organ transplants, leading to serious clinical consequences such as acute and chronic rejection, graft loss, hospital readmissions, and even mortality [1]. Compared with other transplant populations, non-adherence is particularly high among kidney transplant recipients, with reported prevalence ranging widely from 2% to 89% [3,4]. Rates of non-adherence in other organ transplant populations include 42.8% in adult heart transplant recipients [5], 49% in liver transplant recipients [6], and 27.4% in lung transplant recipients [7]. These outcomes underscore the importance of developing and implementing adherence-enhancing interventions—particularly those led by nurses—to reduce non-adherence and promote long-term transplant success.

With the onset of the COVID-19 pandemic, healthcare delivery models rapidly shifted toward digitalization, with remote monitoring and digital health applications gaining prominence in the management of chronic diseases [8]. However, the integration of these technologies into routine practice remains limited [9]. Healthcare professionals often have low levels of awareness regarding the usability and applicability of digital technologies, and insufficient knowledge about available resources contributes to difficulties in adoption [10]. Importantly, there remain significant gaps in the literature regarding the integration of digital health applications into nursing practice and the evaluation of their effectiveness.

This review explores nursing approaches to immunosuppressive medication adherence, drawing upon the current literature.

Causes of Medication Non-adherence

Medication non-adherence can be classified into two categories: intentional and unintentional. Intentional non-adherence occurs when a patient consciously decides not to follow their prescribed regimen, whereas unintentional non-adherence typically results from external factors such as transportation issues, financial difficulties, or lack of access to medications [11].

The World Health Organization (WHO) categorizes the factors influencing medication adherence into five domains: socioeconomic factors, treatment-related factors, patient-related factors, disease-related factors, and health system and healthcare team-related factors [12]. Specific risk factors for non-adherence include being female, younger age, multiple chronic conditions, polypharmacy, inadequate health literacy, lack of information, adverse drug effects, doubts about the importance of immunosuppressive medications, high treatment costs, limited appointment availability, and restricted access to healthcare [4].

Highlights

- Nurse-led interventions play a critical role in improving adherence to lifelong immunosuppressive therapy in transplant recipients
- Multifactorial barriers to adherence can be addressed through educational, behavioral, psychological, and technology-based strategies
- Integration of digital health tools into nursing practice offers promising support for sustained medication adherence

Conversely, protective factors have also been identified. A qualitative study with liver transplant patients revealed that confidence in medications, consistently carrying medications, and receiving family support positively impacted adherence [13]. Similarly, studies with kidney transplant recipients indicated that changes in daily routines were perceived as barriers to medication use [14,15]. Identifying the factors that influence adaptation behaviors is crucial for designing targeted nursing interventions. In particular, recognizing modifiable factors provides the basis for individualized and effective nursing practices [16]. While adherence is often perceived as the sole responsibility of patients, it can be significantly improved through coordinated support from physicians, clinical nurses, pharmacists, and other healthcare professionals.

Assessment and Nursing Approaches in Immunosuppressive Medication Non-adherence

Adherence to immunosuppressive therapy involves not only taking medications but also taking them at the correct dose and time. The first and most critical step in addressing non-adherence is accurate assessment and patient follow-up. Because poor adherence can lead to severe consequences such as organ rejection and increased infection risk, valid and reliable evaluation methods are essential.

A variety of assessment tools have been described, but there is no universal consensus on a standardized approach [11,17]. Methods are generally divided into direct and indirect approaches [12]. Direct methods include directly observed therapy and therapeutic drug monitoring [17]. Although objective and accurate, these methods are limited by cost and feasibility issues [18]. Indirect methods include pill counts, patient self-reports, medication diaries, prescription refill records, and electronic monitoring devices [17]. While easier to apply, indirect approaches may be less reliable [18].

Recently, electronic medication monitoring has become more widespread and is considered a potential gold standard [19]. Tools include electronic pill bottles, smart inhalers, smart blister packs, ingestible sensors, video-observed therapy, electronic medication management systems, mobile health applications, and smartwatches [20]. These technologies enable real-time monitoring and immediate feedback, thereby enhancing adherence. Nonetheless, patient self-reports remain the most widely used method due to their low cost and ease of use [17]. Therefore, a multi-method approach is recommended, as combining different strategies increases accuracy and reliability [12,17,18].

Despite the availability of numerous tools, many healthcare professionals—particularly nurses—report insufficient training in medication adherence assessment [21]. Training programs have been shown to improve nurses' knowledge and evaluation skills in this area [22]. Accurate assessment enables the development of targeted interventions. For example, electronic monitoring has been shown to positively affect adherence to immunosuppressive therapy [23]. Moreover, a meta-analysis demonstrated that multicomponent interventions, particularly those combining electronic monitoring with self-reports, improve patients' knowledge, increase regular participation in follow-up visits, strengthen medication-taking behaviors, and highlight the effectiveness of reminder systems [24].

These findings emphasize the importance of integrating technology-supported monitoring tools into nursing practice to enhance medication adherence in transplant recipients.

The Role of Nursing Interventions in Immunosuppressive Medication Adherence

Nurses are in a unique position to understand patients' daily needs and the challenges they encounter, making them key contributors to clinical decision-making processes [25]. However, they face multiple challenges in improving medication adherence, such as providing patient education, involving caregivers in the educational process, and monitoring medication side effects. Despite these challenges, nurses—who are involved in all stages of healthcare and responsible for delivering holistic care—should play an active role in planning, implementing, and evaluating interventions designed to improve adherence [26]. By identifying the causes of non-adherence, nurses can develop personalized, patient-centered strategies tailored to individual needs and preferences.

In recent years, growing scientific evidence has demonstrated the positive impact of nurse-led interventions on medication adherence [27]. These interventions have been shown to mitigate the adverse consequences of low adherence rates and underscore the critical role of nurses in ensuring patient safety [28]. A large-scale study among European nurses (n=4888) reported that nurses routinely engage in monitoring therapeutic effects and side effects of medications, assessing adherence, managing prescriptions, and providing patient education as integral aspects of their clinical practice [29].

Among the strategies to improve adherence, patient education remains fundamental and should be incorporated into routine clinical practice [30]. Most centers implement structured education programs prior to discharge, covering correct medication use, side effects, the importance of immunosuppressive drugs, diet, weight, blood pressure and temperature monitoring, physical activity, early warning signs of complications, health screenings, and infection prevention. Ideally, education should be reinforced at regular intervals, as single-session education has limited long-term effects [31].

Interventions designed to improve adherence include educational and cognitive approaches, behavioral strategies, psychological and emotional support, financial assistance, electronic monitoring with feedback, and the use of medication reminders [16]. Systematic reviews have shown that psycho-educational programs, outpatient clinic interviews, remote video consultations, structured instructions for medication-taking behaviors, goal setting with action plans, provision of reliable information, health outcome education, feedback, social support, reminder tools, and problem-solving approaches all positively affect adherence [3,32].

A systematic review of randomized controlled trials in transplant recipients found that the most common interventions focused on providing information about health outcomes (78%) and behavior modification (30%) [9]. Psycho-educational interventions are usually delivered by multidisciplinary teams, addressing underlying causes of non-adherence and providing lifestyle guidance. One review highlighted their positive impact on adherence in heart transplant recipients [33]. Although it is difficult to identify the single most effective intervention, evidence suggests that a combination of approaches tailored to patient-specific factors and healthcare contexts is the most successful strategy [3,32]. Given that adherence in chronic disease management is lifelong, nurse-led interventions

should also be designed for long-term implementation. Nonetheless, evidence indicates that adherence often declines over time; for example, De Geest et al. (2014) reported a steady rise in non-adherence between 6 months and 3 years post-transplant [35]. Therefore, sustained monitoring and long-term adherence support are recommended [24].

Despite their central role, many nurses still report gaps in their educational competence. De Baetselier et al. found that 63.4% of nurses did not feel adequately prepared to provide patient education [29]. Strengthening nurses' knowledge and educational skills is therefore essential for improving adherence outcomes. Education not only helps patients recognize potential side effects and seek timely professional support but also shifts the focus from simply remembering to take medications to understanding their critical importance. Evidence suggests that behavioral interventions are often more effective than purely cognitive approaches in improving adherence [36].

Patient motivation is another determinant of adherence, reflecting the willingness to modify behaviors and thought patterns. Motivational interviewing has emerged as an effective strategy for fostering collaboration, setting shared goals, and facilitating behavioral change [37]. Moreover, interprofessional communication and teamwork can further enhance adherence by providing a holistic and consistent approach to medication management.

In recent years, digital health technologies have been increasingly integrated into adherence support. These tools provide significant advantages, including remote monitoring of medication intake, blood pressure, and glucose levels, as well as offering reminders, educational support, and direct communication [30]. Mobile health interventions, in particular, are strongly recommended for optimizing immunosuppressive regimens [24]. Meta-analyses of electronic monitoring interventions have demonstrated significant improvements in adherence [38]. Mobile applications and wearable devices, such as smartwatches, not only deliver reminders but also increase disease awareness, provide education on side effects and drug interactions, and thereby contribute to improved adherence and health outcomes [39].

A Cochrane review assessing interventions to improve immunosuppressive medication adherence in transplant recipients concluded that behavioral strategies, patient education, and digital health applications can be effective. Notably, multicomponent interventions showed the most consistent improvements, although the methodological quality of available studies remains variable [40]. These findings underscore the growing importance of integrating digital health into nursing practice, particularly in managing complex regimens such as lifelong immunosuppressive therapy.

Conclusion

Given that transplant recipients must take immunosuppressive medications throughout their lives, nurses play a pivotal role as the primary link between patients and the healthcare team, especially in education and awareness-raising. Nurse-led, individualized interventions have been shown to improve adherence and, consequently, long-term health outcomes. Strengthening nurses' competencies in adherence assessment through standardized tools, and implementing appropriate interventions in cases of non-adherence, is essential.

Future research should compare nursing interventions across different transplant populations and evaluate the effectiveness of digital solutions. Such studies would provide valuable evidence for refining adherence strategies and advancing nursing practice in the care of organ transplant recipients.

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EUROPEAN TRANSPLANT RESEARCH

REVIEW

Psychiatric comorbidities in pediatric organ transplantation: Current findings and clinical approaches

Begüm Yuluğ Taş,[1] Burcu Özbaran[2]

[1]Department of Child and Adolescent Psychiatry, Tepecik Training and Research Hospital, Izmir, Turkiye
[2]Department of Child and Adolescent Psychiatry, Ege University Faculty of Medicine, Izmir, Turkiye

Abstract

Although pediatric organ transplantation is a critical, life-saving medical intervention that can markedly improve a child's quality of life, it also presents substantial psychosocial challenges for both children and their parents. Psychiatric comorbidities such as anxiety disorders, depression, post-traumatic stress disorder (PTSD), and delirium are frequently observed throughout the transplantation process. Contributing factors include medical uncertainties before and after surgery, prolonged hospitalizations, neuropsychiatric effects of immunosuppressive therapy, and social isolation. Parents similarly face high levels of stress, anxiety, and an increased risk of depression, which can negatively affect family dynamics and financial stability. This review examines the most common psychiatric comorbidities in pediatric transplant recipients, their clinical implications and management strategies, as well as parental psychiatric outcomes, family functioning, and related risk factors. The reviewed studies cover patients from various organ transplant groups and different stages of the transplantation process. Despite heterogeneity across findings, consistent evidence highlights the presence of mental health symptoms in both patients and caregivers. In addition to internalizing and externalizing symptoms, cognitive impairments have also been reported. Post-transplant quality of life in pediatric recipients is influenced by parental well-being, family functioning, transplant type, medication adherence, and pre-transplant mental health status. Thus, focusing solely on medical outcomes is insufficient in pediatric organ transplantation. Emphasizing psychiatric evaluation, multidisciplinary collaboration, and access to psychosocial support is essential to improve adjustment and long-term prognosis.

Keywords: Pediatric organ transplantation, immunosuppression, child and adolescent psychiatry

Organ transplantation is essential for prolonging the lives of patients with organ failure. Neonates, children, and adolescents may all be candidates for organ transplantation, as well as potential donors. Tragically, some children and adolescents die while waiting for an organ transplant, with the highest mortality rate observed among those under one year of age [1]. Since the first successful kidney transplant, solid organ transplantation has become an integral part of pediatric care. Advances in surgical techniques and improvements in immunosuppressive therapies have led to better outcomes and significantly increased long-term survival rates. Currently, the five-year survival rate is over 75% for pediatric heart and liver transplant recipients and over 90% for pediatric kidney transplant recipients [2].

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Correspondence: Begüm Yuluğ Taş, M.D. Department of Child and Adolescent Psychiatry, Tepecik Training and Research Hospital, Izmir, Turkiye
E-mail: yulugbegum@gmail.com
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Pediatric healthcare professionals and mental health specialists play a critical role in addressing the challenges encountered during the organ donation and transplantation process by building trust-based relationships with families and adolescents. They are also uniquely positioned to contribute to shaping public policies related to organ procurement, allocation, and scarcity. Child and adolescent psychiatrists not only provide direct clinical services but also offer counseling to transplant care teams, deliver mental health education, and support care coordination when necessary. They actively participate in the evaluation of potential transplant recipients and monitor post-transplant adaptation and health-related quality of life. Additionally, they address concerns related to informed consent, ethical dilemmas, developmental factors, medication adherence, comorbid psychiatric diagnoses, pain management, and procedural anxiety for patients, families, and the transplant team.

For this purpose, studies involving patients from different organ transplant groups and at various stages of the transplant process were selected. While some studies focus on transplant recipients, others examine the psychiatric effects on caregivers. Although the review primarily covers recent literature, older studies were also included to broaden the evaluation.

Highlights

- Pediatric organ transplantation imposes significant psychosocial burdens on both children and families
- Psychiatric comorbidities in recipients and stress in parents directly affect post-transplant outcomes
- Multidisciplinary psychiatric evaluation and psychosocial support improve adaptation and prognosis

Pre-Transplant Psychiatric Evaluation

During the pre-transplant period, patients undergo comprehensive psychiatric and psychometric evaluations. The primary goals are to enhance understanding of the illness and transplantation process for the patient, parents, and family members; assess the psychiatric suitability of the patient for transplantation; evaluate existing psychosocial support systems; and identify and treat any comorbid psychiatric diagnoses [3].

In this phase, families face numerous challenges, including long waiting times due to the scarcity of organ donations, financial difficulties, stress on siblings and caregivers (due to changing roles and responsibilities), and the burden of complex medical regimens despite the child's ongoing illness [4]. During psychiatric evaluation, the family's socioeconomic status should be considered, and the need for additional support before transplantation should be assessed. If necessary, the assistance of a social worker should be sought.

The presence of comorbid psychiatric diagnoses negatively affects both the course of chronic physical illnesses and the treatment process. Prolonged hospitalizations may create additional stress and challenges not only for the patient but also for family members. While psychiatric comorbidities do not constitute an absolute contraindication for pediatric transplantation, psychiatrists must evaluate factors such as active alcohol or substance use, severe psychopathology, poor medical adherence, risky health behaviors, and inadequate social support. These findings should be carefully discussed by the entire transplant team regarding the appropriateness, feasibility, and timing of transplantation [5].

The transition from hospital to home involves the resumption of physical activity, improvement in dietary habits, return to school, management of potential cognitive deficits, and enhancement of quality of life. Parental and family functioning are directly linked to significant health factors such as adherence to treatment, readiness for discharge, and frequency of hospitalizations [5].

Psychiatrists play a critical role in identifying factors that may affect a family's ability to provide adequate emotional and social support. In this context, they act as a bridge between the transplant team and the family. Parents often experience heightened anxiety and post-traumatic stress symptoms during their child's transplant process. A careful and supportive psychiatric approach can help families better understand their emotional responses and cope with their child's life-threatening illness [3]. High levels of depression and post-traumatic stress in caregivers, as well as family functionality, are closely linked to pre- and post-transplant adaptation [3]. Therefore, psychiatrists should evaluate both the child's knowledge and expectations about their illness and treatment, and the family's functionality and social support network.

Comprehensive developmental history and cognitive assessment are also essential. Children with underdeveloped cognitive functions may not fully understand the transplant procedure and may perceive it as a "punishment." Additionally, these children may experience academic delays due to illness. Cognitive functioning should therefore be assessed in all children with organ failure. For instance, children with congenital heart disease frequently exhibit cognitive and developmental anomalies [6].

The psychosocial status prior to transplantation is strongly associated with post-transplant emotional outcomes. This underscores the importance of early identification and management of psychosocial problems before surgery [7]. A history of alcohol or substance abuse in the patient or family has been linked to a higher risk of substance dependence after transplantation, particularly in adolescent patients who should be carefully evaluated [7]. Identifying comorbid psychiatric conditions plays a vital role in managing the pre-transplantation process and improving post-transplant prognosis, thereby enhancing quality of life [3].

Adherence to treatment for chronic illness before transplantation is an important predictor of post-transplant adherence. Studies have shown that patients who fail to comply with hospital visits and treatments before transplantation are more likely to continue this pattern afterward. Indeed, non-adherence is considered a greater risk factor for poor outcomes than immunosuppression, one of the most common complications [8]. At this stage, adherence to medical treatment is one of the most critical determinants of graft survival. Therefore, identifying risk factors that may affect adherence and addressing them without delay is of paramount importance [9].

Transplantation Process

The transplantation process is a comprehensive sequence consisting of interconnected stages: decision-making and preparation, listing and waiting, surgery and hospitalization, and post-transplant adaptation. The first stage is the decision-making process for organ transplantation and the preparation phase. In this stage, psychiatrists assist the child and parents in making informed decisions. Children typically adapt more easily to the process with the help of clear and understandable explanations from the medical team. The use of transplant education materials during this phase can also be highly effective [4].

Routine health check-ups provide opportunities for proactive guidance, allowing children and adolescents to learn about organ donation and, when appropriate, engage in direct discussions on the topic. During late adolescence, individuals develop a stronger sense of identity and a clearer understanding of their beliefs, values, and priorities. This is a critical phase for making informed and independent decisions, including those related to organ donation. Children and adolescents with intellectual or developmental disabilities should not be excluded from these discussions and should be involved in the process whenever possible [2]. Conditions such as intellectual disability or autism spectrum disorder (ASD) do not constitute definitive contraindications for transplantation. Psychiatric evaluation not only facilitates early identification of potential resistance and risk factors but also ensures ongoing monitoring of patients' coping skills throughout the transplant process [10].

Once the transplant decision is made, the patient is placed on the transplant list, and the waiting process begins. This period often brings intense anxiety for both the child and parents [11]. The duration between being listed and undergoing surgery is uncertain, and during this time medical complications may arise. Therefore, all potential stress factors should be carefully assessed. Additionally, feelings of anger, frustration, and competition may emerge regarding the organ allocation process, further complicating parental coping and increasing their need for psychological support. Financial concerns can also exert significant stress on the family [12].

When a donor is finally found, families often experience mixed emotions, including relief, gratitude, and heightened anxiety regarding the surgical process. Providing psychosocial support at this stage can help families navigate these emotions and manage the process more effectively.

Post-Transplantation Process and Psychosocial Factors

Advances in transplantation medicine have significantly improved allograft function, patient survival, and quality of life. However, transplantation should not be viewed solely as a single surgical event, since post-transplant complications may affect multiple organ systems beyond the transplanted organ itself. Recipients are at a much higher risk than the general population of developing comorbidities such as cardiovascular disease, obesity, infection, malignancy, and chronic kidney disease [2].

In the early post-surgery period or during subsequent hospital readmissions, psychiatrists should be alert to acute changes in mental health. This early phase is particularly challenging as patients undergo intensive medical treatments, often requiring prolonged isolation with a caregiver due to infection risks. Following this stage, adaptation of both the child and family becomes critical. Transplant recipients must adhere to strict treatment regimens, including regular medication use, frequent follow-up visits, and procedures such as biopsies and catheterizations. Some parents describe this experience as "adapting to a new disease called organ transplant" [13].

Beyond physical recovery, the process imposes complex developmental and emotional challenges that create a

significant psychosocial burden on both the child and the family system. Children often struggle to express their fears of rejection, especially if they lack effective coping mechanisms. Anger, guilt, helplessness, and hopelessness are common emotional responses [14]. Psychiatrists must also carefully evaluate the use of psychotropic medications, considering their interaction with immunosuppressive treatments. Corticosteroids, in particular, are well known to induce mood changes and depressive symptoms depending on dosage [15].

Post-transplant, children may also face challenges in adopting their new "healthy" identity, which can negatively affect their academic functioning [16]. Long-term studies on pediatric liver transplant recipients show increased risks of learning difficulties, cognitive delays, and academic setbacks [17]. Moreover, the fact that many transplant recipients come from remote or underserved areas poses challenges for post-discharge care planning. Outpatient psychiatric follow-up may therefore play a critical role in mitigating psychosocial consequences [18].

Psychiatric Conditions After Organ Transplantation in Children and Adolescents

Children who undergo transplantation frequently experience psychiatric conditions, including anxiety, depression, and behavioral problems, though prevalence and presentation vary across studies. Concerns about body image and self-esteem are common in children with chronic physical illnesses and may become particularly pronounced during adolescence, when peer relationships and social acceptance are central [19]. After transplantation, children not only worry about their physical appearance and growth but also about repeated hospitalizations. Prolonged hospitalization often leads to fear of injections, with a higher prevalence among girls [20]. Although such fears rarely interfere with adherence, they represent an important factor for long-term adjustment [21].

In kidney transplant recipients, introverted symptoms and mild behavioral problems have been observed [2]. Similar findings of psychological difficulties have been reported among liver transplant recipients [22]. Conversely, some studies have noted no significant behavioral differences between transplant recipients and healthy peers; for example, one study reported no significant behavioral issues among children post-liver transplantation [23].

Differences in psychiatric outcomes are largely attributed to variables such as gender, age at transplantation, time since transplant, and type of organ transplanted. Studies focusing on younger children suggest that they are more likely to experience elevated parental stress [24], since the medical management of young patients typically falls to parents, increasing the caregiving burden [25]. Younger children also tend to exhibit greater fear and anxiety toward procedures such as blood draws and hospital visits [26]. A recent study of pediatric liver transplant recipients found high rates of depression, anxiety, and post-traumatic stress disorder (PTSD). Interestingly, younger age was negatively correlated with anxiety symptoms [27]. However, other studies found no significant associations between child age, parental stress, or child gender and caregiver stress [28].

Disease stage and treatment duration also strongly influence psychiatric outcomes. For example, children who underwent kidney transplantation after prior hemodialysis showed greater psychiatric distress than those who had not received dialysis [2]. However, other studies have failed to confirm these associations, reporting no significant correlations between illness duration, age at transplantation, years post-transplant, and caregiver burden [29]. Earlier transplant cohorts demonstrated higher psychiatric symptom rates, but more recent multidisciplinary approaches—including psychiatric involvement—appear to have reduced these complications [2].

Psychiatric manifestations in this population are diverse, ranging from delirium and depressive or anxious symptoms to oppositional behaviors, impulsivity, suicidal ideation, enuresis, encopresis, and psychosomatic complaints (e.g., headache, abdominal pain) [30]. Case reports describe depressive mood, anhedonia, and enuresis following heart transplantation [14]. Intensive care admissions also pose risks for delirium, with affected children often requiring prolonged mechanical ventilation, longer hospital stays, and facing lasting motor or behavioral sequelae [31]. Moreover, post-hospital trauma can result in PTSD [32]. A 2021 review (not limited to transplant patients) found PTSD symptoms in 16% of pediatric surgical patients and 23% of parents [32], while more recent reviews specific to transplant recipients confirm a high prevalence of PTSD [33].

Most studies to date have focused on kidney and liver transplant populations, with fewer investigations into heart, lung, intestine, and multi-organ transplant recipients. In lung transplant cohorts, high anxiety rates have been reported, and pre-transplant psychiatric comorbidities were strong predictors of post-transplant difficulties [34]. Likewise, among heart transplant recipients, pre-transplant psychological dysfunction was associated with poorer post-transplant adaptation [6]. While prolonged intensive care stays may delay access to psychiatric support in heart

and lung recipients [35], other studies suggest minimal psychosocial impact following lung transplantation [36].

Cognitive function assessment is critical both before and after transplantation. Children awaiting kidney transplants often exhibit cognitive impairments, but evidence suggests improvements following transplantation, though findings remain limited due to small sample sizes [37]. For example, earlier studies documented both declines in areas such as memory and learning and improvements in domains such as visual perception, verbal ability, and motor skills [38]. Other studies, however, have found persistent deficits in verbal and non-verbal IQ among transplant recipients [39]. Lower IQ scores have been associated with earlier initiation and longer duration of dialysis, as well as older age at transplantation [40]. Pre-transplant conditions such as anemia, prolonged dialysis, and immunosuppressive medications may also constrain post-transplant cognitive recovery [39].

Even before dialysis or transplantation, children with chronic kidney disease (CKD) are at heightened risk of academic failure [41]. This risk often persists after transplantation, affecting long-term educational and vocational outcomes. In one cohort, 9 out of 12 young adults with kidney transplants failed to complete college [42]. Executive function deficits—including difficulties in problem-solving, attention regulation, working memory, inhibition, and cognitive flexibility—are common. Mendley et al. reported improvements in processing speed, discrimination sensitivity, and working memory among medically stable pediatric kidney recipients [43]. However, more recent studies have demonstrated significant declines in processing speed post-transplant, especially in children transplanted at an older age (≥80 months) [38].

The findings are summarized in Table 1.

Family Dynamics and Parental Stress

Parents of children with chronic illnesses experience higher levels of parenting stress compared to parents of healthy children. Although pediatric transplant recipients were not included in some of these studies, research consistently shows that parental stress negatively affects children's mental health [44]. Elevated parental stress has also been linked to lower adherence to immunosuppressive medications after transplantation. In contrast, families with healthier functioning—both parents and adolescents—encounter fewer adherence barriers such as forgetfulness, scheduling difficulties, or intentional nonadherence [45].

The transplantation process profoundly affects not only children but also their families. Studies indicate that nearly one-third of parents of pediatric transplant recipients develop symptoms of PTSD, regardless of the type of transplantation [46]. Similarly, parents of children who required a ventricular assist device (VAD) prior to heart transplantation reported high levels of anxiety and depressive symptoms [47]. Evidence suggests that caregivers with effective coping skills enhance both psychiatric adjustment and quality of life for transplant recipients [48]. Therefore, providing psychosocial support to parents as well as to transplant recipients is critical for parental mental health and the child's prognosis.

Increased family conflict has been associated with externalizing behavioral problems and reduced quality of life in children after kidney transplantation [44]. A large-scale review also confirmed that parental stress has a negative effect on medication adherence [3]. Family functioning is closely related to hospitalization and discharge preparation. Weaker family bonds have been shown to predict higher hospitalization rates, explaining 10.24% of the variance [44]. Minimizing disruptions to family routines and lifestyles has been associated with improved quality of life [49]. Nevertheless, some studies report no deterioration in family functioning post-transplant [50]. A supportive family environment reduces children's stress and may protect against psychiatric comorbidities [51].

Two separate studies with parents of pediatric liver transplant candidates found that stress levels were high before transplantation [52]. These findings were linked to family burden, financial strain, and disrupted family dynamics. Another study found that parents' anxiety levels were higher than their children's [20]. However, a long-term study of parents of liver transplant recipients (≥4 years post-transplant) reported that the disease's negative impact on family functioning was lower than in other pediatric chronic illness groups [53]. Conversely, another study with parents of liver transplant recipients 5–6 years post-transplant found that they experienced more financial difficulties, poorer coping, and a greater burden on siblings compared to families of children with other chronic diseases or disabilities [26].

Taken together, these findings highlight the importance of viewing the family as a whole and conducting psychosocial assessments before transplantation. Early evaluation enables the activation of social support systems before and during the transplant process. Evidence shows that pre-transplant social support and higher family quality of life contribute to better post-transplant survival outcomes [54].

The findings are summarized in Table 2.

Table 1. Psychiatric Conditions Following Organ Transplantation in Children and Adolescents

Study	Organ Type	Results
Reynolds et al. (1991)[2]	Kidney	It has been found that individuals receiving hemodialysis experience greater psychiatric effects compared to those who do not undergo this treatment. These effects can include both internalized symptoms, such as anxiety and depression, as well as externalized behaviors, such as aggression.
Henning et al. (1988)[21]	Kidney	Fear and anxiety during the transplantation process have been shown to affect long-term adjustment in patients.
Lullmann O et al. (2017)[37]	Kidney	Executive functions tend to decline post-transplantation, with factors such as receiving a transplant at an older age, having additional medical conditions, and long treatment durations playing a significant role in this decline.
Harshman et al. (2019)[41]	Kidney	Even before the need for dialysis or transplantation arises, children with chronic kidney disease are at risk of academic failure.
Murray et al. (2019)[42]	Kidney	It has been observed that patients' academic functionality continues to decline even after transplantation.
Mendley & Zelko (1999)[43]	Kidney	Improvements have been reported in the transplant patients' processing speed, reaction time, discrimination sensitivity, and working memory.
House et al. (1983)[22]	Liver	It was found that all children who underwent liver transplantation were affected psychiatrically.
Alonso et al. (2013)[23]	Liver	Although parents were affected after transplantation, they did not report behavioural symptoms towards their children.
Kaller et al. (2014)[26]	Liver	It was observed that frequent blood collection procedures and hospital appointments were quite challenging for both children and parents, and younger children were affected more frequently.
Duken&Yayan (2024)[27]	Liver	In liver transplant recipients, symptoms of depression, anxiety, and PTSD were observed to be prominent, and a negative correlation was found between the recipient's age and anxiety levels
Ozbaran et al. (2024)[10]	Heart	Although accompanying behavioural disorders in children with intellectual disability and autism do not constitute a contraindication for heart transplantation, they may constitute an obstacle for devices such as ventricular assist devices applied during the transplantation process.
Çelik et al. (2019)[14]	Heart	Depressive mood, anhedonia and enuresis were observed after heart transplantation.
Fedewa et al. (1996)[29]	Kidney and Liver	However, no significant relationship was found between pre-transplant disease duration, transplant age, years passed since transplantation, hospitalization frequency, and the caregiving burden on the family.
Lee JM et al. (2017)[40]	Kidney and Liver	The prolonged treatment process has been shown to contribute to cognitive impairments.
Penner et al (2022)[20]	Kidney, Liver and Heart	It has been observed that children develop a fear of injections as a result of prolonged hospital follow-up.
Ucgun&Cıtak (2024)[33]	Kidney, Liver and Heart	Children who have undergone organ transplantation, PTSD was found to be prevalent
Wilson et al. (2016)[34]	Lung	It was found that anxiety levels were high and pre-transplant psychiatric status was an important factor in predicting the post-transplant process.
Bujoreanu et al. (2015)[35]	Heart and Lung	It was observed that long intensive care stay after transplantation delayed psychiatric evaluation.
Hirshfeld et al. (2004)[36]	Heart and Lung	The results showed that there was no psychiatric effect after transplantation.

PTSD: Post-traumatic stress disorder.

Conclusion

Pediatric organ transplantation, while a life-saving intervention that improves quality of life, imposes substantial emotional, psychological, and social burdens on both children and their families. Psychiatric comorbidities such as anxiety and depression are common in children during this process. Key risk factors include medical uncertainties before and after transplantation, prolonged hospitalizations, neuropsychiatric effects of

Table 2. Parent and family functioning in pediatric organ transplantation

Study	Organ Type	Results
Cousino et al. (2017)[3]	Multiorgan Transplant	Parental stress was found to have a negative effect on medication adherence.
Simons et al. (2007)[28]	Multiorgan Transplant	The stress burden of parents during the transplantation process was not related to the age of their children.
Young et al. (2003)[46]	Multiorgan Transplant	Parents showed PTSD symptoms after transplantation, but the type of transplantation was not found to be effective in this.
Soliday et al. (2001)[44]	Kidney	It was observed that parental stress and family conflicts adversely affected child mental health and increased the number of hospitalisations.
Gerson et al. (2004)[45]	Kidney	It was observed that parents and adolescents with healthy family functioning experienced less obstacles such as forgetfulness and programming problems in medication use.
Fukunishi et al. (1995)[50]	Kidney	It was determined that there was no deterioration in family functioning after transplantation.
Soliday et al. (2000)[49]	Kidney	It has also been shown that a suitable family environment can reduce the stress of the child during the transplantation process and prevent additional psychiatric diagnoses.
Kaller et al. (2014)[26]	Liver	It was observed that experiencing great financial difficulties during the transplantation process affected the family's coping process more.
Denny et al. (2012)[49]	Liver	It was observed that changes in family lifestyle decreased the quality of life.
DeBolt et al. (1995)[53]	Liver	In a study conducted with patients 4 years after transplantation, it was reported that the negative impact of the disease on the family system was lower compared to other paediatric chronic disease groups.
Trzepacz et al. (1992)[54]	Liver	It has been shown that social support received before transplantation and high quality of life levels increase survival rates after transplantation.
Ozbaran et al. (2012)[47]	Heart	High anxiety and depressive symptoms were observed in parents of children with VADs.
Yılmaz Kafalı et al. (2021)[48]	Heart	Healthy coping skills of caregivers increase psychiatric adaptation and quality of life of transplant recipient children.
Penner et al (2022)[20]	Kidney, Liver and Heart	It has been observed that the anxiety levels of parents are higher than those experienced by their children.

PTSD: Post-traumatic stress disorder.

immunosuppressive therapies, and social isolation. In parallel, parents face high levels of stress, anxiety, and depression, which can disrupt family dynamics and compromise financial stability.

Therefore, focusing solely on medical outcomes in pediatric organ transplantation is insufficient. Ensuring access to psychosocial support mechanisms is essential for families. Evidence demonstrates that psychiatric evaluations of children and multidisciplinary support approaches positively influence post-transplant adjustment and prognosis. Future research should emphasize the evaluation of psychosocial interventions and the development of improved strategies to promote mental health in pediatric transplant patients.

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