Development and Psychometric Testing of the Turkish Immunosuppressive Medication Adherence Scale

İmmünsupresif İlaç Kullanımına Uyum Ölçeğinin Geliştirilmesi ve Psikometrik Özelliklerinin İncelenmesi

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ABSTRACT

OBJECTIVE: The monitoring of immunosuppressive medication adherence is an important issue for solid organ transplant patients. There has been no valid and reliable measurement tool developed in Turkey for transplant patients for the evaluation of medication adherence. This methodological study aims to develop and psychometrically test the Immunosuppressive Medication Adherence Scale.

MATERIAL and METHODS: The Immunosuppressive Medication Adherence Scale was developed and its validity and reliability were evaluated using data from 200 solid organ transplant patients. An expert panel evaluated the content validity, and factor analysis was used to evaluate the construct validity. Internal consistency analysis was performed to evaluate the reliability of the scale and item-total correlations were evaluated.

RESULTS: As a result of exploratory factor analysis, all eleven items were found to be collected in a single dimension and factor loadings varied between .32 and .87. All scale items had a good positive significant correlation with the total scale score. Content validity was evidenced by obtaining the views of 13 experts (0.80 CVI). Cronbach's α was .61.

CONCLUSION: The Immunosuppressive Medication Adherence Scale has acceptable internal consistency, good content and construct validity. The scale is appropriate for use in clinical practice settings and research to evaluate immunosuppressive medication adherence of solid organ transplant patients.

KEY WORDS: Immunosuppressive agents, Medication adherence, Organ transplantation, Scale development

ÖZ

AMAÇ: Solid organ transplantasyonu yapılan hastalarda immünsupresif ilaç kullanımına uyumun değerlendirilmesi önemli bir konudur. Türkiye'de transplant hastalarına özgü geliştirilmiş, ilaç kullanımına uyumu değerlendiren geçerli ve güvenilir bir ölçüm aracı bulunmamaktadır. Bu metodolojik çalışmada İmmünsupresif İlaç Kullanımına Uyum Ölçeğinin geliştirilmesi ve psikometrik özelliklerinin test edilmesi amaçlanmıştır.

GEREÇ ve YÖNTEMLER: İmmünsupresif İlaç Kullanımına Uyum Ölçeği solid organ transplantasyonu yapılan 200 hastadan elde edilen veriler doğrultusunda geliştirilmiş, geçerliliği ve güvenilirliği test edilmiştir. Kapsam geçerliliğinin değerlendirilmesinde uzman görüşlerine başvurulmuş, yapı geçerliliğinin değerlendirilmesinde faktör analizi yöntemi kullanılmıştır. Ölçeğin güvenilirliğinin değerlendirilmesinde ise iç tutarlılık analizi ve madde-toplam korelasyon hesaplamaları yapılmıştır.

BULGULAR: Açıklayıcı faktör analizi sonuçlarına göre 11 ölçek maddesinin tek boyutta toplandığı ve maddelerin .32 ile .87 arasında faktör yüklenmelerinin olduğu belirlenmiştir. Tüm ölçek maddeleri toplam puan ile pozitif anlamlı korelasyon göstermektedir. Kapsam geçerliliği 13 uzman görüşü ile sağlanmıştır (0.80 içerik geçerlilik indeksi). Cronbach's α .61 olarak hesaplanmıştır.

SONUÇ: İmmünsupresif İlaç Kullanımına Uyum Ölçeğinin kapsam ve yapı geçerliliği sağlanmıştır ve kabul edilebilir bir iç tutarlılığa sahiptir. Ölçeğin, solid organ transplantasyonu yapılan hastaların immünsupresif ilaç kullanımına uyumunu değerlendirmede klinik ortamda ve araştırmalarda kullanımı uygundur.

ANAHTAR SÖZCÜKLER: İmmünsupresif ilaç, İlaç uyumu, Organ transplantasyonu, Ölçek geliştirme

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INTRODUCTION

The aims of immunosuppressive treatment in solid organ transplantation are to prevent graft rejection, maintain graft function, lengthen graft and patient survival durations, and increase the patient's quality of life. The fact that organ transplant patients have to use multiple immunosuppressive drugs continuously or for many years causes difficulties with medication adherence. Various adherence rates for immunosuppressive drug use have been reported for organ transplant patients (1-3). According to a meta-analysis, the rate of immunosuppressive medication adherence in all transplantation types was 19-25% (1). Another study reported an immunosuppressive medication adherence rate of 37.9% for a sample comprising patients with heart, lung, kidney, and liver transplants (2). Furthermore, medication adherence in patients who had undergone heart, lung, and liver transplantation has been found to vary between 23.9% and 70% (4).

Medication adherence is defined by the World Health Organization as 'the extent to which the patient's behaviour coincides with the clinical prescriptions' (5). Medication adherence means that the drug prescribed is used consistently according to the time, dose, and frequency recommended by the health professional during the period determined. Medication nonadherence is present when the drugs are not taken at the specified dose, time, and interval, and when doses are missed or postponed, or not taken at all (2,5-9). Nonadherence is an important factor that negatively affects the success of treatment and quality of life, and increases the costs of health care. To prevent graft rejection, lengthen graft and patient survival durations, and increase the patient's quality of life, the evaluation of medication adherence using standard measurement methods is imperative. Various methods are used in the evaluation of medication adherence. These methods are classified as direct and indirect methods. Direct methods include drug concentration monitoring, monitoring of metabolite levels in the blood or urine assays, and observing directly that the patient takes the drug. Indirect methods include interviewing the patient, self-report, counting tablets, monitoring prescription records, electronic monitoring, patient journals, questionnaires, and interviewing patient relatives (5,9-16). The self-report method is feasible, uncomplicated and inexpensive so it is considered as the most practical and convenient method to evaluate medication adherence. Self-report is also one of the best measures of adherence for the detection of both missed doses and erratic timing of medication (7,9,17). Each of the direct and indirect methods has advantages and disadvantages. Therefore, using a combination of the current methods is usually recommended to evaluate adherence, instead of a single method (7,12,17). It has been shown that combining self-reporting, assay, and a clinician's report yielded the highest sensitivity and specificity compared to electronic monitoring (16). There are only a few valid, reliable, and globally applicable measurement tools for evaluating immunosuppressive medication adherence that are specifically designed for patients who have undergone solid organ transplantation. No valid and reliable measurement tool that is specific to the transplantation field has been found in Turkish. A valid and reliable measurement tool for Turkish solid organ transplant patients is needed. Therefore, we developed an immunosuppressive medication adherence scale for evaluating adherence in solid organ transplant patients so that nonadherence could be identified at an early stage in order to prevent the development of relevant complications and problems.

METHODS

Study Design

The study was conducted as a methodological study in order to develop and psychometrically test an immunosuppressive medication adherence measure for solid organ transplant patients.

Setting and Sample

The study was conducted at a university hospital's organ transplantation centre in Ankara, Turkey, between January 2015 and July 2015. Participants comprised adult and adolescent transplant patients who had sufficient responsibility to administer their immunosuppressive medication, and ability to use the drugs without help; participants were being followed-up at the organ transplantation centre. The number of participants included in the study sample was calculated using the item number × patient number formula (10-30 patients required for each item in the scale). Therefore, the study sample needed to include at least 10 patients for each item of the scale (20 × 10 = 200) (18,19). The numbers of heart, liver, and kidney transplant patients in the total sample were determined by stratified sampling (proportional sample allocation) of the number of patients who had undergone solid organ transplantation and were being followed-up at the hospital where the study was conducted. Accordingly, 150 kidney transplant patients, 35 liver transplant patients, and 15 heart transplant patients were included. The study sample inclusion criteria were identified as: (a) aged 13 years and over, (b) having completed the second month of follow-up after solid organ transplantation, (c) ability to use the drugs without help, (d) lack of any problem preventing communication, (e) lack of a psychological or mental problem, and (f) agreeing to participate in the study. Data from face-to-face interviews (lasting on average 20-25 minutes) was collected by the investigator. An information sheet was used to gather sociodemographic and medical information data, and the Immunosuppressive Medication Adherence Scale was administered.

Scale Development Process

The Immunosuppressive Medication Adherence Scale was developed based on the instrument development guidelines by DeVellis and Tezbasaran (Figure 1) (20,21).

Initial Item Development

The views of experts in the transplant field and patients who had undergone solid organ transplantation were obtained. A semi-structured questionnaire with four open-ended questions for experts (definition and measurement of medication adherence, kinds of medication adherence problems, and reasons for medication nonadherence) and four open-ended questions for patients (definition of medication adherence, kinds of challenges of using immunosuppressives, methods of using immunosuppressives regularly, reasons for medication nonadherence) was developed by the investigator after a literature review. The semi-structured questionnaire was administered in face-to-face interviews with 40 patients who had undergone solid organ transplantation (10 heart, 15 kidney, and 15 liver transplantations) and 10 specialists (three organ transplantation coordinators, four transplantation nurses, and three physicians working in the field of transplantation). A literature review regarding the subject was performed to determine the characteristics to be measured. The expressions to be potentially included in the scale were written in accordance
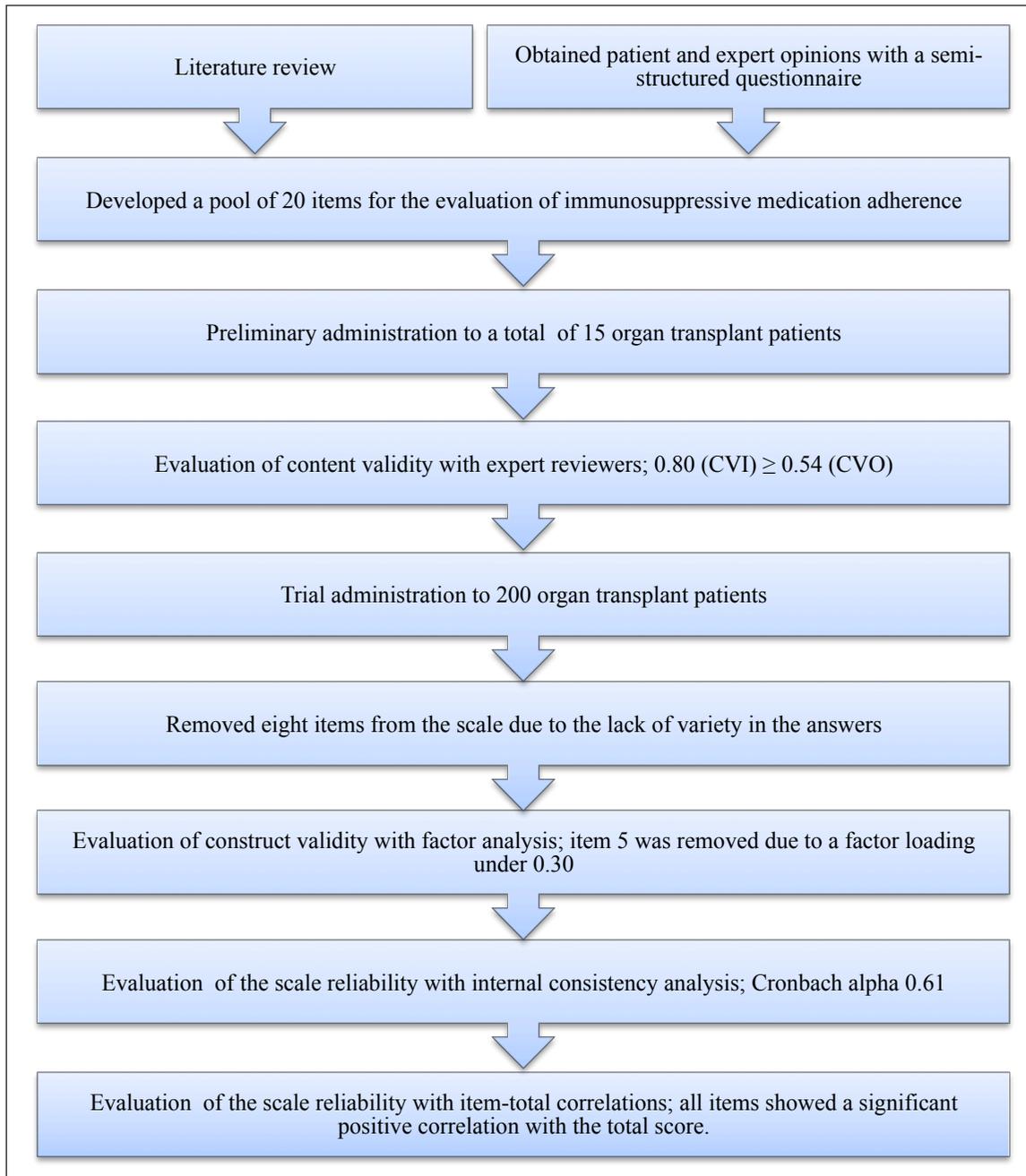

Figure 1: *The immunosuppressive medication adherence scale development process.*

with the data obtained from the semi-structured questionnaires and the literature review; a pool of 20 items for the evaluation of immunosuppressive medication adherence was developed. Likert-type grading (5-point and 2-point scales) was used when scoring. Individuals selected the statement they found appropriate from 'yes' and 'no' for the 2-point scale type, and from the expressions 'never', 'rarely', 'sometimes', 'often', and 'always' for the 5-point scale.

Preliminary and Trial Administration

The scale and information sheet were administered to a total of 15 patients who had undergone a total of eight kidney, five liver, and two heart transplantation procedures and who were using immunosuppressive drugs at transplantation outpatient departments. The clarity and applicability of the scale and information sheet were tested during the preliminary administration. The final version of the scale was administered to 200 patients that met the inclusion criteria at transplantation outpatient departments.

Scale Validity

Content validity and construct validity measurement methods were used as a validity criterion method in order to determine whether the Immunosuppressive Medication Adherence Scale accurately reflected the measured characteristics. Expert reviewers assessed the content validity of the Immunosuppressive Medication Adherence Scale. Factor analysis was used to evaluate construct validity. Exploratory factor analysis (EFA) was used to reveal the dimensional structure of the measurement tool when analysing categorical data. The weighted smallest squares method, based on polychoric and tetrachoric correlations, was used in the analysis of categorical data, considering the answer categories of the items (22). Items with a factor loading under 0.30 were removed from the measurement tool. Medication adherence statistics were used when deciding the number of dimensions necessary for the items included in the measurement tool.

Scale Reliability

Internal consistency analysis was used to evaluate the reliability of the scale. Cronbach's α was calculated as a prediction of internal consistency of the measurement tool (23). Additionally, item-total correlations were calculated.

The Instrument

A pool of 20 items for the evaluation of immunosuppressive medication adherence was first developed. Eight items in the scale were not appropriate for the measurement of the desired characteristic and the statistical analysis; thus, due to the lack of variety in the answers they were directly removed from the scale. One item (item number 5) was eliminated following analysis of the validity and reliability of the 12-item scale, leaving 11 items in the final version of the scale. Likert-type grading (5-point and 2-point scales) was used. One point was an indicator of a negative attitude and 5 points indicated a positive attitude in both the 5-point and 2-point scales. The minimum and maximum scores that can be obtained from the scale of 11 questions were 11 and 55, respectively.

Ethical Considerations

Ethical approval was obtained from a university ethics committee (dated 28.11.2014, no. 99950669/345) and permission was received from the university hospital where the study was conducted. Furthermore, informed consent was obtained from participants and the parents of adolescent patients aged 13-18 years after the aims of the study and the voluntary nature of participation were explained and confidentiality was ensured in accordance with the Helsinki Declaration.

Statistical Data Analysis

The SPSS for Windows version 11.5 (SPSS Inc. Chicago, IL, USA) software programme was used for the evaluation of the data and the statistical analysis. Regarding descriptive statistics, frequency and percentages were used for the categorical data and arithmetic mean ± standard deviation were used for the continuous variables. Cronbach's α and item-total score correlations were calculated in the reliability analysis of the scale. Construct validity of the scale was investigated using EFA. The MPlus 6.1 trial version was used for the administration of the EFA (24). The statistical significance limit was accepted as .05.

RESULTS

Participant Characteristics

The mean age of the 200 participants was 36.95 ± 13.9 years, with 37% ($n = 74$) in the 35-49 years age group and 14.5% ($n = 29$) in the 13-19 years age group. Males made up 57.0% ($n = 114$) of all participants, 57.0% ($n = 114$) were married, and the educational level was primary school in 48.0% ($n = 96$). The transplanted organ was the kidney in 75.0% ($n = 150$) of participants, the liver in 17.5% ($n = 35$), and the heart in 7.5% ($n = 15$). Transplantation was performed from a living donor in 70.0% ($n = 140$) of cases. The time since transplantation was 0-2 years in 36.5% ($n = 73$) of participants, and 3-9 years in 46.0% ($n = 92$) of participants. Prednisolone was used by 87.5% ($n = 175$). Mycophenolate mofetil was used by 54.0% of participants, tacrolimus was used by 53.5%, and a combination of three drugs was used by 81.0% ($n = 163$) (Table I).

Validity Analysis

Content Validity

Expert reviewers evaluated the content validity. A total of 20 items were submitted for review by 13 experts. The experts evaluating the content validity consisted of three pharmacists, one kidney-liver transplant surgeon, one heart transplant surgeon, one nephrologist, one cardiologist, one gastroenterologist, one specialist in surgical nursing, one specialist in internal medicine

Table I: Characteristics of Participants (N=200)

Characteristics	Number	%
Age		
(Min=13, Max=65, average=36.95±13.9)		
13-19	29	14.5
20-34	57	28.5
35-49	74	37.0
50-65	40	20.0
Gender		
Female	86	43.0
Male	114	57.0
Marital Status		
Married	114	57.0
Single	86	43.0
Educational Status		
Primary school	96	48.0
High school	57	28.5
University and above	47	23.5
Transplanted organ		
Heart	15	7.5
Liver	35	17.5
Kidney	150	75.0
Donor Type		
Cadaveric donor	60	30.0
Living donor	140	70.0
Time since transplantation		
(Min=3 months, Max=19 years, average=5.3±4.5 years)		
0-2 years	73	36.5
3-9 years	92	46.0
10 years and above	35	17.5
Immunosuppressive drugs used*		
Prednisolone	175	87.5
MMF	108	54.0
Tacrolimus	107	53.5
Mycophenolate Sodium	70	35.2
Cyclosporine	44	22.0
Sirolimus	37	18.5
Everolimus	8	4.0
Azathioprine	4	2.0
Immunosuppressive drug type used		
Single drug	13	6.5
Two drugs combined	25	12.5
Three drugs combined	162	81.0

*N was doubled and the percentages determined according to N.

nursing, one Turkish language specialist, one assessment-evaluation specialist, and one biostatistics specialist. The experts were asked to grade each item as 'necessary', 'useful, but insufficient', or 'unnecessary', and to explain their reasons for suggesting changes and marking any items as 'unnecessary'.

After receiving the experts' reviews, the content validity ratio (CVR) was calculated for each item using the following formula, where N_G is the number of experts who chose the "necessary" option and N is the total number of experts (25).

$$CVR = \frac{N_G}{N/2} - 1$$

According to the formula, items yielding a CVR value of zero or less were removed from the scale. For items with a positive score, only those with a level of significance of α = .05 or greater were retained, in order to simplify calculations. Accordingly, the minimum CVR was calculated as 0.54; there were no items with a CVR score lower than 0.54 in the final scale. Finally, the content validity index (CVI) of the 20-item scale was calculated. To calculate the CVI, the formula CVI = ΣCVR/item number was used (25). The CVI calculated for the 20 items was 0.80, and the content validity of the scale was found to be statistically significant with a result of 0.80 (CVI) ≥ 0.54 (CVO).

Construct Validity

When the answers received after the trial administration were investigated, eight of the items were found not to be appropriate due to the lack of variety in the answers given; these were excluded from the statistical analysis. EFA was used for the categorical data, revealing a dimensional structure that consisted of 12 items after the eight items were eliminated. The factor loadings of the variables were evaluated to reveal the structural characteristic of the variables in the EFA. When the factor loadings of the items were investigated, they were found to vary between 0.32 and 0.87. We ensured that the items had a minimum factor loading of 0.30. Item number 5 (Do you ever not take your immunosuppressive drugs with you while you go out or during travel?) had a factor loading under 0.30 and was removed from the measurement tool at this stage. The items and their factor loadings are presented in Table II.

Reliability Analysis

Internal consistency analysis was used to evaluate the scale's reliability and item-total correlations were investigated. The Cronbach's α calculated for the 11 remaining items was 0.61. When item-total correlations were investigated, all items included in the scale were found to show a significant positive correlation with the total score. Item-total correlations are presented in Table III.

DISCUSSION

A standardized scale should have the two properties of reliability and validity. This study psychometrically tested the immunosuppressive medication adherence scale to investigate whether the scale could be used as a standard measurement instrument. The total scale score of each participant consists of the total of answers given to each item in the Likert-type scale.

Table II: Factor Loadings of the Immunosuppressive Medication Adherence Scale Items.

Order	Items	Factor Loads
1	Item 1: Do you ever forget to take your immunosuppressive drug?	0.47
2	Item 2. Do you ever quit taking immunosuppressive drugs without consulting your physician when you feel good?	0.87
3	Item 6. Do you ever interrupt taking immunosuppressive drug or miss the dose due to your daily activities (such as school or work)?	0.33
4	Item 9. Do you take your immunosuppressive drug you forgot to take immediately when you remember (within 2-3 hours)?	0.58
5	Item 11. Do you ever delay purchasing new ones when your immunosuppressive drugs are finished?	0.72
6	Item 12. Do you adjust the time you take your immunosuppressive drugs according to your meal times?	0.48
7	Item 13. Do you ever interrupt taking your drugs because using immunosuppressive drugs every day challenges you?	0.71
8	Item 14. Do you ever interrupt taking your drugs because using multiple immunosuppressive drugs challenges you?	0.73
9	Item 16. Considering the past two weeks, have you ever taken your immunosuppressive drug doses less than recommended?	0.78
10	Item 18. Considering the past two weeks, have you ever missed/ skipped your immunosuppressive drug dose?	0.32
11	Item 19. Considering the past two weeks, have you ever received your immunosuppressive drug a couple of hours earlier or after the normal time?	0.43

Table III: Immunosuppressive Medication Adherence Scale Item-Total Correlations.

Scale Item No	Total Score	
	r	P
Item 01	0.41	0.001
Item 02	0.41	0.001
Item 06	0.45	0.001
Item 09	0.45	0.001
Item 11	0.46	0.001
Item 12	0.44	0.001
Item 13	0.65	0.001
Item 14	0.42	0.001
Item 16	0.48	0.001
Item 18	0.38	0.001
Item 19	0.58	0.001

Therefore, all items should be scored. Scoring varies depending on whether an item is positive or negative. The negative items are scored inversely to positive items. Thus, high scale scores always show a positive attitude (21). Both 5-point and 2-point Likert-type scoring were used in this study.

Validity and Reliability

Content Validity

The content validity was investigated to determine whether the items adequately represented the immunosuppressive medication adherence of solid organ transplant patients (26,27). The initial 20-item scale, prepared according to the results obtained from the semi-structured questionnaire and literature review, was submitted to 13 experts for review. At the end of the content analyses, the validities for the 20-item scale were provided with a result of 0.80 CVI.

Construct Validity

Construct validity is demonstrated by the degree to which the measurement tool correctly captures the desired concept, and the degree to which scale items relate to the factor(s) they attempt to measure (26,27). The most commonly used construct validity method is factor analysis (21,27). This method was also used in the evaluation of the construct validity of the scale. The EFA was conducted for the categorical data in order to reveal the dimensional structure of the 12-item scale measurement tool. The factor loadings of the variables were evaluated with this analysis and the items were found to collect along a single dimension. Despite different views regarding what the factor loads should be, it is generally reported that this value should be at least 0.30 (26,27). The items, with the exception of item number 5 that was removed from the scale, had a minimum

factor load of 0.30. In conclusion, to ensure construct validity, it was decided that the most appropriate analysis according to the items and factor loadings was a single-factor structure.

Scale Reliability

Reliability is an indicator of how effectively the items included in a measurement tool consistently measure the characteristic in relation to each other (21,27). Various techniques can be used for the calculation of scale reliability, and one is chosen according to the study conditions and aims (26). Internal consistency analysis was conducted to evaluate the reliability of the scale and item-total correlations were investigated. Cronbach's α is recommended to determine the reliability of a Likert-type scale. It is a measure of the internal consistency of scale items (21,23) and it is more valuable when focusing on measuring a single characteristic and a single factor. The alpha value for each dimension should be calculated separately in scales with more than one dimension. The EFA that was performed over the 12 items revealed that the items collected along a single dimension. The Cronbach's α calculated for the 11 remaining items, after one item was eliminated due to a low factor loading, was 0.61. The evaluation threshold of Cronbach's α can vary according to the qualification of the criterion (20,26,28,29). According to the criterion employed to evaluate the alpha coefficient, the following were used: $0.00 \leq \alpha < 0.40$ indicated that the scale is not reliable, $0.40 \leq \alpha < 0.60$ indicated that the scale has low reliability, $0.60 \leq \alpha < 0.80$ indicated that the scale is quite reliable, and $0.80 \leq \alpha < 1.00$ indicated that the scale is highly reliable (30). Also, Cronbach's α of greater than or equal to 0.6 was interpreted as acceptable by methodologist (28,29). Item-total correlations were also investigated within scale reliability and all of the scale questions were found to have a significant positive correlation with the total score (Table III). The internal consistency coefficient and item-total correlations indicated that the scale was reliable.

Clinical Usage of the Turkish Immunosuppressive Medication Adherence Scale

The evaluation of medication adherence using standard measurement methods is imperative in the transplant clinical settings, to prevent graft rejection and lengthen graft and patient survival durations. Self-report is considered as the most practical and inexpensive method to evaluate medication adherence for the detection of both missed doses and erratic timing of medication (7,9,17). In the Turkish society, there is a critical need to identify nonadherent transplant recipients with a feasible and uncomplicated self-report scale. This study provides a non-invasive, valid and reliable instrument that measures immunosuppressive medication adherence as needed in the clinical settings. When the patients visit the outpatient clinic, the scale can be completed easily and quickly by the patients. It can provide valuable information about nonadherent patients and give an opportunity to health professionals to identify reasons of

nonadherence. The Immunosuppressive Medication Adherence Scale should be used with other indicators of adherence such as immunosuppressant serum concentrations and graft organ function tests.

Limitations: The inclusion of three different transplantation groups (heart, liver, and kidney) in the sample groups created a limitation in terms of sample homogeneity. It is thought that Cronbach's α is .61 because of the involvement of three different organ transplant patients in the study.

CONCLUSION

Based on the data obtained from the study, the Immunosuppressive Medication Adherence Scale was shown to be valid and reliable for the evaluation of immunosuppressive medication adherence in solid organ transplant patients. This scale is recommended in the evaluation and follow-up of medication adherence in Turkish patients who have undergone solid organ transplantation, and in studies for determining the rates of medication adherence of patients who use immunosuppressive drugs. Furthermore, studies testing the scale's validity and reliability in other countries could be performed within the scope of cultural adaptation research, and it could be used in clinical environments and studies in the relevant countries after the adaptation studies are conducted.

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