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Evaluation of Adherence with Immunosuppressive Treatment and Symptom Occurrence of in Patients with Kidney Transplantation

Böbrek Transplantasyonu Yapılan Hastaların İmmunsupresif Tedaviye Uyum ve Semptom Oluşma Durumunun Değerlendirilmesi

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Özet

Amaç: Tanımlayıcı ve ilişkisel bir çalışma olan bu araştırma, böbrek nakli hastalarının immünsupresif tedaviye uyumunu, semptom oluşumunu ve bu faktörler arasındaki ilişkiyi belirlemeyi amaçlanmıştır.

Yöntem: Çalışmamızda, Hasta Tanıtım Formu, İmmünsupresif İlaç Kullanımına Uyum Ölçeği ve Modifiye Transplantasyon Sonrası Semptom Oluşma ve Rahatsızlık Formu-58 kullanılmıştır. Araştırmanın evrenini Ankara'da bir hastanenin 2023 Ocak-Nisan tarihlerinde Nefroloji Polikliniğine tedavi, kontrol veya bakım için gelen böbrek transplantasyonu olmuş bireyler oluşturmaktadır. Çalışmamızın örneklemini böbrek transplantasyonu olmuş 125 birey oluşturmaktadır. Veriler; Frekans analizleri, Mann-Whitney U testi, Kruskal-Wallis H testi, Bonferroni düzeltmesi, Spearman korelasyon katsayısı kullanılarak değerlendirilmiştir.

Bulgular: İmmunsupresif ilaç kullanımı uyum ölçeği puanları arttıkça, semptom oluşumu ve semptom sıkıntısı azalmaktadır. Cinsiyete göre semptom sıkıntısı puanları açısından istatistiksel olarak anlamlı farklılık tespit edilmiştir (Z=-2.491; p=0.013). Kadınların semptom sıkıntısı puanlarının erkeklere göre anlamlı düzeyde daha yüksek olduğu, ek hastalık durumuna göre semptom oluşumu puanları (Z=-2.425; p=0.015) ve semptom sıkıntısı puanları (Z=-2.415; p=0.016). açısından istatistiksel olarak anlamlı farklılık tespit edildiği belirlenmiştir. Donör tipine göre semptom oluşumu puanları açısından istatistiksel olarak anlamlı farklılık tespit edilmiştir (Z=- 1.983; p=0.047). Çalışmada en sık görülen semptomlar kendini yorgun hissetme, ruh halinde dalgalanma ve ellerde titreme olarak belirlenmiştir. En çok sıkıntı veren semptomlar ruh halinde dalgalanma, huzursuzluk veya gerginlik yaşam durumu ve kendini yorgun hissetme olarak belirlenmiştir.

Abstract

Aims: This research, a descriptive and relational study, aims to determine kidney transplant patients' adherence with immunosuppressive therapy, their symptom occurrence, and the relationship between these factors.

Methods: We used the Patient Introduction Form, Immunosuppressive Medication Adherence Scale, and Modified Transplant Symptom Occurrence and Distress Form-58 in our study. The population for the study consisted of 125 individuals with kidney transplantation who attended the Nephrology Outpatient Clinic of a hospital in Ankara between January and April 2023 for treatment, follow-up or care. Data were evaluated using frequency analysis, Mann-Whitney U test, Kruskal-Wallis H test, Bonferroni correction, and Spearman correlation coefficient.

Results: Increased scores on the immunosuppressive drug use adherence scale correlated with decreases in symptom occurrence and distress. A statistically significant difference was found in symptom distress scores according to gender (Z=-2.491; p=0.013), with women exhibiting significantly higher scores than men. Statistically significant differences were also detected in terms of symptom occurrence scores (Z = -2.425; p = 0.015) and symptom distress scores (Z = -2.415; p = 0.016) according to comorbidity. Additionally, a statistically significant difference was found in symptom occurrence scores according to additional disease status (Z=-2.425; p=0.015), and in symptom distress scores according to additional disease status (Z=-2.415; p=0.016). A statistically significant difference was found in terms of symptom occurrence scores according to donor type (Z=-1.983; p=0.047). The most common symptoms in the study were feeling tired, mood swings and tremors in the hands. The most distressing symptoms were mood swings, restlessness or nervousness, and feeling tired.

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Sonuç: Çalışmanın sonucu; immunsupresif ilaç kullanımı uyum ölçeği ile semptom oluşumu ve semptom sıkıntısı arasında negatif yönde, zayıf derecede ve istatistiksel olarak anlamlı ilişki tespit edilmiştir ($p<0.05$).

Anahtar Kelimeler: Böbrek transplantasyonu; Hemşirelik; İmmunsupresif tedavi; Semptom sıkıntısı; Tedaviye uyum.

Conclusion: A negative, weak, and statistically significant relationship was observed between the immunosuppressive drug use adherence scale scores with symptom occurrence and symptom distress ($p<0.05$).

Keywords: Kidney transplantation; Nursing; Immunosuppressive therapy; Symptom distress; Medication adherence.

INTRODUCTION

In patients with life-threatening end-stage organ failure, transplantation new and healthy organs from a live donor or cadaver to replace organs injured to the degree where they cannot function is called transplantation (Tx) (1). Kidney transplantation (KTx) is the foremost treatment choice for end-stage kidney disease due to lengthening the patient's life expectancy, increasing quality of life and providing more effective outcomes in the long term (2).

Immunosuppressive treatment (IST), one of the treatment methods used after transplantation, prevents rejection of the transplanted organ by suppressing the immune system (3). Lack of adherence with immunosuppressive drugs is accepted as an important factor in graft rejection and graft loss (4). As a result, it is important that patients fully comply with IST after KTx is performed.

Side effects from mandatory post-transplantation immunosuppressive drugs can sometimes negatively impact patients. Studies researching the effects of drugs used after transplantation identified that physical symptoms like fatigue, muscle weakness, excessive appetite increase, backache and headache, pruritis, dizziness, diarrhea and feeling thirsty were experienced (5, 6). At the same time, these patients experienced several psychological and emotional symptoms like depression, irritability, fatigue and hand tremors (6). It is important that nurses know and understand these symptoms developing linked to immunosuppressive drugs after transplantation better in terms of improving the quality of life of individuals (7). Enhancing quality of life and drug adherence in post-transplant patients requires reducing symptoms and providing effective symptom management. (8). The main target of care, the most important role in nursing, is to reduce symptoms felt by the patient and protect the patient by making treatment adherence easier (9). In the study conducted by Schmid-Mohler et al. (10) the use of medications in kidney transplant patients was examined and it was observed that non-adherence with treatment increased as the years of use increased. The reason for this situation is thought to be the high level of adherence of patients with treatment in the first years due to the comfort of just getting rid of dialysis. Situations such as the belief that the transplanted organ adapts to the transplanted organ and that the body will not reject the kidney in the subsequent processes, the belief that the medication used over the years will provide protection throughout life, and the possibility of repeat transplantation reduce patients' adherence with the treatment over time and increase the frequency of experiencing symptoms. Nurses undertake important duties in ensuring symptom management for individuals with chronic disease and play a large role in patient care (11). The aim of this research, based on this key role, is to determine the adherence with immunosuppressive treatment of patients with kidney transplantation and to determine symptom occurrence and identify the relationship between adherence and symptoms.

Research Questions

1. What is the level of adherence with immunosuppressive treatment of patients with kidney transplantation?
2. What are the symptom occurrence and symptom discomfort levels of patients with kidney transplantation?

3. Is there a correlation between immunosuppressive treatment adherence total scores with sociodemographic data?
4. Is there a correlation between symptom occurrence and symptom discomfort total scores with sociodemographic data?
5. Is there a correlation between immunosuppressive treatment adherence total scores with symptom occurrence and symptom discomfort total scores?
6. What are the most common symptoms according to Ridit analysis?
7. What are the most common symptoms causing distress according to Ridit analysis?

MATERIAL AND METHODS

Type of Research

The study is descriptive and relational in nature.

Population and Sample of the Research

The population for the research comprised individuals with kidney transplantation attending as outpatients at the nephrology clinic of an education and research hospital in Ankara from January-March 2023. The study included individuals aged 18 years and older, with at least two months since kidney transplantation, who voluntarily agreed to participate in the research. As a result of power analysis to determine the sample number, with 0.05 significance level, 0.3 effect size, and 95% power, the sample required 111 individuals and 125 was determined as the sample number.

Data Collection Tools

Research data were collected with the Patient Introduction Form, Immunosuppressive Medication Adherence Scale (IMUAS) and Modified Transplant Symptom Occurrence and Distress Form 58 (MTSOSD-58TR).

Patient Introduction Form: This form for individuals participating in the research comprised 10 questions about age, sex, drugs used, marital status, duration since transplantation, educational level, comorbid diseases, donor type, person assisting with drug use and receiving education related to immunosuppressive drug use. The patient introduction form was created after investigating references in the literature (12-14).

Immunosuppressive Medication Adherence Scale (IMUAS): This was developed by Özdemir Köken, Talas and Gökmen (13) with the aim of assessing adherence to immunosuppressive drug use by patients with solid organ transplantation. The scale comprises 11 items in a single dimension and rating uses 5-point and 2-point Likert scoring. Items with 5-point Likert rating are given points from 1 to 5 for positive items and 5 to 1 for negative items. Items with yes-no answers are given points of 1 for yes and 5 for no. Positive statements are given in items 4 and 6, while items 1, 2, 3, 5, 7, 8, 9, 10 and 11 are negative statements. The minimum points that can be obtained are 11, while maximum points are 55. The increase in points obtained from the scale shows increased adherence with immunosuppressive drug use. Özdemir et al. calculated the Cronbach alpha value as 0.611 (13). In this research, the Cronbach alpha value was 0.713.

Modified Transplant Symptom Occurrence and Distress Form 58 (MTSOSD-58TR): The original form developed by Dobbels et al. (15) comprised 59 items and was called the MTSOSD-59. All items on the scale assess a side effect of immunosuppressive drugs and each item has two dimensions assessing symptom occurrence and distress. On the scale, items labelled “a” indicate symptoms, while items labelled “b” indicate distress. The symptom occurrence dimension assesses the symptom frequency and intensity (0=never, 4=all the time), while the symptom distress dimension assesses the degree of discomfort the symptom causes the individual (0=no discomfort, 4=excessive discomfort). Twenty-three patients with symptom occurrence score of 0 received symptom distress score of 0 and were not included in the assessment (12). The validity and reliability study in Türkiye was performed by Ordin, Karayurt and Çilengiroğlu (16). The study was performed with 100 liver and 80 kidney transplant patients and 180 people not using immunosuppressive drugs. The results of face

validity for the scale found it had very good face validity (16). Internal consistency coefficients are not calculated as the items on the scale are not homogeneous. Ridit analysis was used to determine the most frequent symptoms of transplantation patients. A fall in Ridit value shows that symptoms are observed less, while an increase in Ridit value shows the incidence of symptoms is increased (16). Ridit values are between 0 and 1. There is a need for a reference group to be able to compare symptoms or distress (16). The reference group in the research used data from the reference group in the study by Sarıgöl Ordin (with permission) (17).

Data Analysis

Statistical analyses were completed using the SPSS program (IBM SPSS Statistics 27). Frequency tables and descriptive statistics were used to interpret findings. "Shapiro-Wilk" test for subgroups where the sample size is fifty or less; For those fifty and over, normality distribution was determined according to the "Kolmogorov Smirnov" test statistics. Measurement values without normal distribution used non-parametric methods. In accordance with non-parametric methods, comparison of measures in two independent groups used the Mann-Whitney U test (z-table value), and comparison of measures in three or more independent groups used the Kruskal-Wallis H test (χ2-table value). Two-way comparisons of significant variables in three or more groups used the Bonferroni correction. Investigation of the relationships between two quantitative variables without normal distribution used the Spearman correlation coefficient. The Excel 21 program was used to calculate Ridit analysis scores.

Ethical Considerations

To implement the research, a thesis proposal form was organized and the necessary ethics committee project approval was obtained from Ankara Yıldırım Beyazıt University Health Sciences Ethics Committee (dated 06.10.2022, decision number 14). Permission to be able to perform the research in the relevant institution was obtained from Ankara Governorship, the Provincial Directorate of Health, and Ankara City Hospital with Education Planning Committee permission no. 3 dated 23.12.2022, permit no. E-90739940-799-206271696 and permit no. E-36198255-149927-135186 dated 27.10.2022, respectively, obtained via Ankara Yıldırım Beyazıt University Health Sciences Institute. Permission to use the scales was obtained by email from the relevant authors. After explaining the aim of the study, importance and the survey forms to participants, they were told their personal information would be kept confidential and that personal information included on the scales would not be given to anyone other than the researcher. All participants provided informed written and verbal consent.

RESULTS

The mean age of patients participating in the study was 46.83±11.89 years. Of these, 69 people (55.2%) were 40-59 years old, 80 people (64.0%) were men, 92 people (73.6%) were married and 64 people (51.2%) were primary school graduates. Among the study sample, 102 people (81.6%) were on a triple regime (tacrolimus), Fifty-two people (41.6%) had more than 60 months since the transplant and 84 people (67.2%) had comorbidities. For patients, 76 (60.8%) had live donor, 110 people (88.0%) had no assistance with drug use and 70 people (56.0%) had not received education about drug use.

When Table 1 is investigated, the IMUAS total mean score was 48.99±4.39 for individuals participating in the research. The minimum points on the scale are 11, with maximum points of 55. The mean scores from the scale were high for individuals participating in the research. The MTSOSD-58TR scale symptom occurrence total mean score for individuals participating in the study was 34.08±24.85, with symptom distress total mean score of 21.56±26.69. In this study, it was important to determine symptom frequency and the most common symptoms, rather than the mean scores for symptom occurrence and symptom distress. There was a negative, weak and statistically significant correlation identified between IMUAS scores with symptom occurrence and symptom distress ($p<0.05$). As the IMUAS scores increased, symptom

occurrence and symptom distress decreased. Similarly, as the IMUAS scores reduced, symptom occurrence and symptom distress increased (Table 1).

When the findings in the research are investigated by comparing scale scores, there were no statistically significant differences for symptom occurrence, symptom distress and IMUAS scores according to age, marital status, educational level, drugs used, person assisting drug use, education about drug use and duration since transplantation (months) (p>0.05). According to sex, there were no statistically significant differences for symptom occurrence and IMUAS scores (p>0.05), while a significant difference was identified in terms of symptom discomfort scores (Z=-2.491; p=0.013). Women were identified to have higher symptom distress scores compared to men at a significant level. According to comorbid diseases, there was no statistically significant difference in terms of IMUAS scores (p>0.05). A statistically significant differences was identified for symptom occurrence scores according to comorbid disease status (Z=-2.425; p=0.015). Those with comorbid diseases had higher symptom occurrence scores at a significant level compared to those without comorbid disease. In terms of symptom distress scores, there was a statistically significant difference according to comorbid disease (Z=-2.415; p=0.016). The symptom distress scores of those with comorbid diseases were determined to be higher at a significant level compared to those without comorbid disease. There were no statistically significant differences for symptom distress and IMUAS scores according to donor type (p>0.05). A statistically significant difference was identified in terms of symptom occurrence scores according to donor type (Z=-1.983; p=0.047). Symptom occurrence scores for those with cadaver donor were determined to be high by a significant level compared to those with living donor (Table 2).

Table 1. Correlations Between Scales and Score Distribution

Correlation* (N=125)			**Immunosuppressive Drug Use Adherence Scale**
Modified Post Transplantation Symptom Occurrence and Discomfort Form	*Symptom occurrence*	*r* *p*	-0.254 **0.004**
	Symptom discomfort	*r* *p*	-0.195 **0.029**

Scale (N=125)		**Mean**	**SD**	**Median**	**Min.**	**Max.**
Immunosuppressive Drug Use Adherence Scale		48.99	4.39	50.0	34.0	55.0
Modified Post Transplantation Symptom Occurrence and Discomfort Form	*Symptom occurrence*	34.08	24.85	28.0	1.0	166.0
	Symptom discomfort	21.56	26.69	13.0	0.0	17.0

*Spearman correlation coefficient used to investigate correlations of two quantitative variables without normal distribution
*Min: Minimum, Max: Maximum, SD: Standard Deviation, r: Spearman's Correlation Test

Table 2. Comparison of Scale Scores According to Research Findings

Variable (N=125)	n	Modified Post Transplantation Symptom Occurrence and Discomfort Form				Immunosuppressive Drug Use Adherence Scale	
		Symptom occurrence		*Symptom discomfort*			
		$\bar{X} \pm S.D.$	Median [IQR]	$\bar{X} \pm S.D.$	Median [IQR]	$\bar{X} \pm S.D.$	Median [IQR]
Age class							
<40	36	30.86±21.13	23.5 [23.3]	18.28±22.03	11.0 [24.3]	48.64±4.79	49.5 [7.8]
40-59	69	35.30±24.36	30.0 [31.0]	23.12±25.37	17.0 [27.5]	48.93±4.42	49.0 [4.0]
≥60	20	35.65±32.51	30.5 [14.8]	22.10±37.69	13.0 [15.8]	49.85±3.54	50.0 [5.3]
Statistical analysis*		Σ^2=1.103		Σ^2=2.407		Σ^2=0.831	
Probability		p=0.576		p=0.300		p=0.660	
Sex							
Male	80	30.90±21.25	27.0 [20.0]	17.51±22.05	11.0 [20.3]	48.64±4.72	49.0 [5.0]
Female	45	39.73±29.64	38.0 [32.5]	28.76±32.41	20.0 [33.5]	49.62±3.70	50.0 [6.0]
Statistical analysis		Z=-1.837		Z=-2.491		Z=-1.837	
Probability		p=0.066		**p=0.013**		p=0.066	
Marital status							
Married	92	34.08±23.18	28.0 [28.8]	20.73±24.53	12.5 [24.8]	48.84±4.43	49.0 [4.0]
Single	33	34.09±29.41	29.0 [25.5]	23.87±32.27	14.0 [28.0]	49.43±4.31	50.0 [6.0]
Statistical analysis		Z=-0.462		Z=-0.552		Z=-0.277	
Probability		p=0.644		p=0.581		p=0.782	
Education level							
Primary school/lower	68	33.41±26.26	29.0 [27.5]	20.90±27.37	13.0 [24.8]	49.60±4.22	50.0 [7.0]
Middle school	17	34.59±20.87	27.0 [25.0]	18.75±24.63	11.0 [26.5]	49.06±4.43	50.0 [6.0]
High school	26	38.96±27.46	33.5 [35.5]	27.62±30.56	16.0 [32.0]	47.77±4.09	48.5 [6.5]
Associate degree/higher	14	27.64±15.94	24.5 [21.3]	16.93±16.70	12.5 [19.8]	48.21±5.45	49.0 [5.5]
Statistical analysis		Σ^2=3.488		Σ^2=2.140		Σ^2=2.683	
Probability		p=0.322		p=0.544		p=0.443	
Drugs used							
Triple regime	106	33.23±23.69	28.0 [26.3]	20.82±25.80	12.0 [25.0]	48.81±4.51	49.0 [4.3]
Double regime	9	34.00±18.05	34.0 [21.5]	19.22±14.89	15.0 [22.5]	50.44±3.74	51.0 [4.0]
Sirolimus/Everolimus	10	43.20±39.59	25.5 [53.5]	31.50±41.55	16.0 [45.0]	49.60±3.50	50.5 [4.8]
Statistical analysis*		Σ^2=0.293		Σ^2=0.598		Σ^2=1.818	
Probability		p=0.864		p=0.741		p=0.403	
Transplant duration (months)							
2-12	25	30.00±21.48	24.0 [30.5]	15.24±18.59	6.0 [26.0]	50.12±4.18	51.0 [6.5]
13-24	16	36.81±35.95	29.5 [18.0]	26.25±41.61	17.0 [15.0]	48.00±4.12	48.0 [4.5]
25-36	10	49.70±34.82	39.0 [39.5]	34.80±43.32	21.0 [41.8]	47.90±4.75	49.5 [6.8]
27-48	8	40.38±24.73	34.5 [45.0]	22.25±19.66	16.5 [38.5]	49.88±2.53	50.0 [3.3]
49-60	14	37.36±29.88	36.0 [35.8]	30.07±33.79	24.0 [34.5]	50.93±3.24	51.0 [4.8]
>60	52	30.34±17.25	27.5 [20.8]	18.21±17.09	13.0 [19.8]	48.31±4.83	48.0 [5.8]
Statistical analysis		Σ^2=4.985		Σ^2=4.477		Σ^2=7.422	
Probability		p=0.418		p=0.485		p=0.191	
Comorbid disease							
Yes	84	37.63±27.34	33.0 [28.5]	25.17±29.91	17.0 [27.3]	48.76±4.66	49.0 [4.0]
No	41	26.80±16.80	23.0 [18.0]	14.17±16.38	11.0 [14.0]	49.46±3.79	50.0 [6.0]
Statistical analysis		Z=-2.425		Z=-2.415		Z=-0.531	
Probability		**p=0.015**		**p=0.016**		p=0.595	

*For data without normal distribution, Mann-Whitney U test used for comparison of two independent groups (z-table value); Kruskall-Wallis H test used for comparison of three or more independent groups (χ^2-table value)

*Σ^2: Kruskal Wallis H Test, $\bar{X} \pm S.D.$: Mean ± Standard Deviation

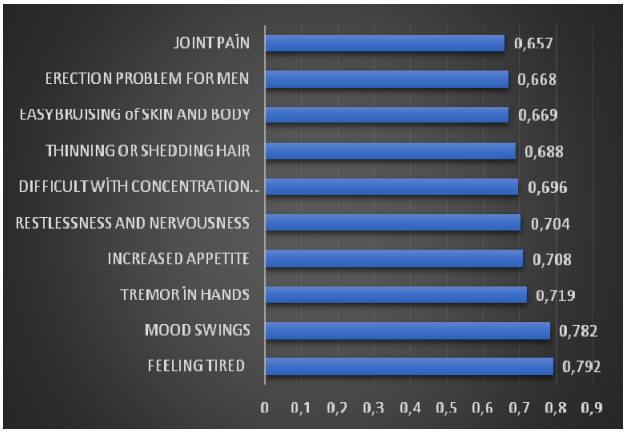
Table 2 (cont.). Comparison of Scale Scores According to Findings in the Research

Variable (N=125)	n	Modified Post Transplantation Symptom Occurrence and Discomfort Form				Immunosuppressive Drug Use Adherence Scale	
		Symptom occurrence		*Symptom distress*			
		$\bar{X} \pm$ S. D.	Median [IQR]	$\bar{X} \pm$ S. D.	Median [IQR]	$\bar{X} \pm$ S. D.	Median [IQR]
Donor type							
Cadaver	49	37.63±24.24	34.0 [24.0]	23.67±26.27	15.0 [28.5]	50.04±3.44	50.0 [5.5]
Live	76	31.79±25.13	25.5 [25.3]	20.19±27.03	11.0 [25.5]	48.32±4.80	49.0 [5.0]
Statistical analysis		Z=-1.983		Z=-1.366		Z=-1.840	
Probability		**p=0.047**		p=0.172		p=0.066	
Assistance with drugs							
Yes	15						
No	110	47.07±41.49	39.0 [33.0]	38.20±46.95	26.0 [36.0]	47.60±5.72	48.0 [9.0]
		32.30±21.33	28.0 [25.3]	19.29±21.99	12.0 [24.3]	49.18±4.17	50.0 [5.3]
Statistical analysis		Z=-1.292		Z=-1.935		Z=-0.748	
Probability		p=0.196		p=0.053		p=0.454	
Education about drugs							
Yes	55	33.87±24.14	27.0 [24.0]	21.07±24.58	13.0 [25.0]	49.16±4.59	50.0 [6.0]
No	70	34.24±25.58	30.0 [25.8]	21.94±28.40	13.5 [25.3]	48.86±4.25	49.0 [4.3]
Statistical analysis		Z=-0.251		Z=-0.199		Z=-0.805	
Probability		p=0.802		p=0.842		p=0.421	

*For data without normal distribution, Mann-Whitney U test used for comparison of two independent groups (z-table value); Kruskall-Wallis H test used for comparison of three or more independent groups (χ^2-table value)

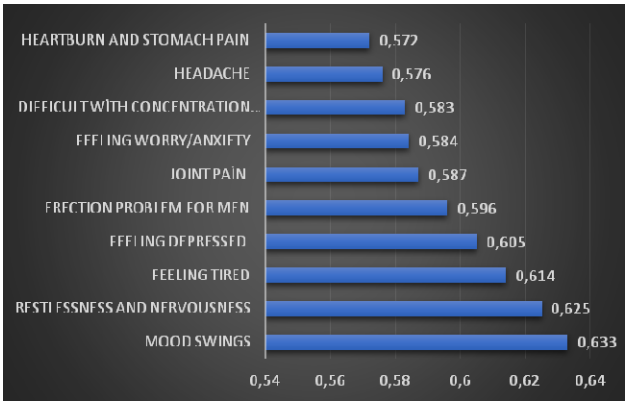
*Σ^2: Kruskal Wallis H Test, $\bar{X} \pm$ SD: Mean ± Standard Deviation

The most frequent 10 symptoms for individuals participating in the research were calculated according to Ridit analysis and shown in Graph 1.



Graph 1. Symptom occurrence ridit values

The 10 most distressing symptoms among individuals participating in the research were calculated according to Ridit analysis and are shown in Graph 2.



Graph 2. Symptom distress ridit values

DISCUSSION

This study was performed with the aim of assessing the immunosuppressive treatment adherence and symptom occurrence in patients with kidney transplantation. When the correlation between MTSOSD-58TR and IMUAS is examined, there was a negative, weak and statistically significant correlation identified. As the scores for the immunosuppressive drug use adherence scale increased, symptom occurrence and symptom distress reduced.

After transplantation, patients must remain on a single, double or triple treatment regime of immunosuppressive drugs. In studies in the literature, a triple treatment regime administering tacrolimus or cyclosporin comes to the fore in terms of immunosuppressive treatment regime (7, 13, 14, 16). In this study, similar to the literature, there were high levels of triple treatment regime use (81.6%). In our study, 60.8% of patients received kidney transplantation with living donor grafts. Wang et al. (18) identified 57% living donor graft receivers in their study, while the study by Bunthof et al. (19) identified 70.2% were living donor graft receivers. The reason for the high living graft receivers for kidney transplantation is thought to be the scarcity of cadaver organ donations, very high chance of living a normal and healthy life with a single kidney based on human anatomy and that KTx can be performed from person to person.

The increase in points obtained from the scale shows that the individual has increased immunosuppressive drug use adherence. A study by Köken et al. (20) found the mean IMUAS score was 48.10±6.61 for transplantation patients. Ordin et al. (14) found the mean IMUAS score for transplantation patients was 48.66±4.71. Akbulut et al. (21) found the IMUAS mean score in a study of Tx receivers was 41 for those with hepatocellular carcinoma (HCC) and 43 for those without HCC. In our study and in studies in the literature, Tx recipients must use immunosuppressive medication to avoid organ rejection. However, in the literature there are studies which found low levels of adherence to immunosuppressive drug adherence (22, 23). It is thought that the adherence or lack of adherence of transplantation receivers to immunosuppressive drugs may vary linked to education received after transplantation, symptoms experienced and social support received. There were no statistically significant differences in terms of age, sex, marital status, comorbid disease, educational level, donor type, drugs used, transplant duration, person assisting drug use, education about drugs and IMUAS total mean scores for KTx patients participating in the study ($p>0.05$). In our study, the mean drug adherence score for KTx patients was 48.99±4.39.

In our study, according to the MTSOSD-58TR scale, the total mean score for symptom occurrence in KTx patients was 34.08±24.85 with symptom distress mean score of 21.56±26.69. In our study, female Tx receivers were found to have higher symptom burden compared to male Tx patients (28.76±32.41). In the literature, there are studies with the distribution of symptom occurrence and symptom distress mean scores according to sex. The study by Kim and Jang (12) found male Tx receivers had symptom occurrent total mean score of 52.14±22.0, while this value was 72.18±25.59 for female Tx receivers. The mean symptom distress scores were 48.98± 23.11 for men and 75.77±25.29 for women (12). Ordin et al. (16) found the mean symptom occurrence total score was 88.78±20.51 and mean symptom distress total score was 84.75±19.23 for Tx cases. For male Tx patients, the total mean symptom occurrence score was 85.23±16.24, while this value was 93.32±24.29 for female Tx patients. In terms of mean symptom distress scores, values were 81.16±14.27 for men and 89.24±23.44 for women (16). In our study, the meant total score for symptom occurrence in male Tx receivers was 30.90±21.25, with score of 39.73±29.64 for female Tx receivers. The mean symptom distress scores were 17.51±22.05 for men and 28.76±32.41 for women. In our study, a statistically significant difference was identified for symptom distress scores according to sex ($Z=-2.491$; $p=0.013$). Women were found to have higher symptom distress scores by a significant level compared to men. Literature studies observed that female Tx receivers had higher total mean

scores for symptom distress (12, 16). The results lead to consideration that female Tx receivers are more sensitive to drug side effects and this situation causes higher mean symptom distress score.

In kidney transplantation patients, different comorbid diseases apart from kidney disease negatively affect the symptom and distress status after Tx for these patients. According to comorbid disease status in our study, there was a statistically significant difference identified in terms of symptom occurrence scores (Z=-2.425; p=0.015). Those with comorbid disease were determined to have higher symptom occurrence scores at a significant level compared to those without comorbid disease. In terms of symptom distress scores, a statistically significant difference was identified according to comorbid disease status (Z=-2.415; p=0.016). The symptom distress scores for those with comorbid disease were determined to be higher by a significant level compared to those without comorbid disease. This situation leads to negativities for KTx patients like quality of life, inadequacy meeting self-care needs, and use of multiple drugs due to immunosuppressive drugs and drugs for comorbid diseases. The use of immunosuppressive drugs after transplantation and drugs linked to comorbid diseases and negative aspects of comorbid disease are thought to cause more symptom occurrence and symptom distress in KTx patients.

Kidney transplantation may be performed in two ways; living donor to living patient and cadaver to living patient. The transplanted organ is obtained from a living donor or a cadaver. In our study, 60.8% were living donor graft receivers for kidney transplantation. In our study, there was a statistically significant difference identified in terms of symptom occurrence scores according to donor type (Z=-1.983; p=0.047). Those with cadaver donor were determined to have higher symptom occurrence scores by a significant level compared to those with living donors. While the organ is transplanted within minutes for Tx performed from living donor to living receiver, it takes generally hours to transplant organs obtained from cadavers. This causes a lengthened period of cold ischemia and it is thought that symptom occurrence is high linked to this lengthened duration for cadaver Tx receivers (24).

In our study, the symptoms with most frequent occurrence on the MTSOSD-58TR scale were identified to be feeling tired, mood swings, tremor in hands, increased appetite, restlessness and nervousness, difficulty with concentration and/or recall, thinning or shedding hair, easy bruising of skin and body, erection problems for men and joint pain. The most distressing symptoms were mood swings, restlessness and nervousness, feeling tired, feeling depressed, erection problems for men, joint pain, feeling worry/anxiety, difficulty with concentration and/or recall, headache, and heartburn and stomach pain. In a study of patients with liver transplantation by Ordin et al. (16), the ten most common symptoms were excessive sweating, fatigue, facial swelling (moon face), tremor in hands, increased appetite, muscle weakness, and increased body and facial hair. The same study found the ten symptoms causing highest levels of distress were excessive sweating, facial swelling (moonface), tremor in hands, increased appetite, anxiety, thinning or shedding of hair, fatigue, mood swings, muscle weakness, and increased facial and body hair (16). The most frequent symptoms in the study by Kim and Jang (12) were fatigue, lack of energy, thinning or shedding hair, erectile problems in men, and wounds on lips or mouth. The most distressing symptoms were fatigue, lack of energy, thinning/shedding hair, erectile problems in men, swelling of feet or ankles and back pain. The study by Wang et al. (18) found the most frequent symptoms were fatigue, lack of energy, difficulty falling asleep, loss of appetite, dry skin, and swelling. The most frequent distressing symptoms were lack of energy, loss of appetite, excessive sweating, weakness in muscles, and fatigue (18). The use of double or triple immunosuppressive drugs in transplantation patients is thought to negatively affect systems in the body of Tx receivers causing symptom occurrence and distress. In our study and according to results from studies in the literature, immunosuppressive drugs cause negative side effects in the gastrointestinal system, circulation system, nervous system, musculoskeletal system and

skin of Tx patients. To ensure adherence with immunosuppressive drugs and the negative aspects caused by these side effects, it is necessary to closely monitor the symptom occurrence and distress levels of Tx patients. It should also be added a suggestion that evidence-based practices with proven effectiveness can be planned for symptom management.

CONCLUSION AND SUGGESTIONS

There were high levels of immunosuppressive treatment adherence among patients with kidney transplantation. Medication adherence scale scores increased, symptom occurrence and symptom distress scores reduces.

According to Ridit analysis, the most common symptoms were feeling tired, mood swings, tremor in hands, increased appetite, restlessness and nervousness, difficulty with concentration and/or recall, thinning or shedding of hair, easy bruising of skin and body, erection problems for men and joint pain.

According to Ridit analysis, the most frequent distressing symptoms were mood swings, restlessness and nervousness, feeling tired, feeling depressed, erection problems in men, joint pain, feeling worried/anxious, difficulty with concentration and/or recall, headache and heartburn and stomach pain.

Based on these results, we recommend that

KTx patients and relatives be given education to prevent symptoms and distress that may occur before and after kidney transplantation,

The importance of adhering to immunosuppressive treatment and risks that may emerge linked to not using drugs regularly should be explained to KTx patients in detail and training should be organized. For assessment before and after this training, randomized controlled studies about knowledge, adherence and symptom management should be performed.

Comprehensive training should be given to prevent patients skipping routine follow-up and check-ups after transplantation and discharge education should be given in an understandable way.

Qualitative studies should be performed to be able to more effectively investigate the topic and to determine symptoms that may occur and drug incompatibility.

ETHICS COMMITTEE APPROVAL

Ankara Yıldırım Beyazıt University Health Sciences Ethics Committee (date: 06.10.2023, decision no. 14).

INFORMED CONSENT

Informed consent was obtained from study participants

CONFLICT OF INTEREST

No financial or other conflict of interest is present in relation to the study.

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PEER REVIEW

External independent, double blind.

AUTHOR CONTRIBUTIONS

Idea, design: MA, Bİ

Plan: MA, Bİ

Data collection: MA, Bİ

Analysis: MA, Bİ

Article writing: MA, Bİ

Critical review: MA, Bİ

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