



## The relationship between polypharmacy and quality of life in kidney transplant patients

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Received: 29.03.2024

Accepted/Published Online: 16.09.2024

Final Version: 30.09.2024

### Abstract

Chronic kidney disease (CKD) is becoming more widespread globally. Thanks to renal replacement therapy (RRT) methods, the life expectancy of CKD patients is gradually increasing. Today, the notion of quality of life has come to the forefront in evaluating treatment efficacy with increasing life expectancy. Among the RRT methods, kidney transplantation is the one that improves the quality of life the most. Polypharmacy is a concept that has been on the agenda recently and is known to have adverse effects on quality of life. Kidney transplant patients are frequently exposed to polypharmacy due to immunosuppressive drugs and comorbidities, particularly during the initial stages of transplantation. In our study, the KDQOL-SF questionnaire was administered to 128 kidney transplant recipients who visited the Nephrology outpatient clinic between October 2023 and November 2023. Those taking  $\geq 6$  medications were defined as the group exposed to polypharmacy. Polypharmacy was considered present in 74 of the patients involved in the study. The mean age of the patients was  $51.8 \pm 11.5$  years in the polypharmacy group and  $42.4 \pm 12.5$  years in the non-polypharmacy group. In renal transplant patients, the quality of life was notably reduced in the polypharmacy group. The presence of polypharmacy showed a statistically significant correlation with age, comorbidity, multimorbidity, marital status, and primary disease. The group with polypharmacy had notably lower scores in all sub-parameters of the KDQOL-SF. In conclusion, our study determined that the presence of polypharmacy had a negative impact on the quality of life of renal transplant patients. Polypharmacy was found to be associated with age, comorbidity and multimorbidity.

**Keywords:** kidney transplantation, polypharmacy, quality of life, renal replacement

### 1. Introduction

The prevalence of chronic kidney disease (CKD) is on the rise due to the increasing elderly population world population. However, the number of patients developing end-stage renal disease (ESRD) is also increasing(1). Treatment methods used to replace lost kidney function relatively are called renal replacement therapy (RRT). The RRT method that improves quality of life the most is renal transplantation(2).

The drug burden in renal transplant patients is relatively high, especially in the early stages of transplantation(3). In renal transplant recipients, immunosuppressive agents often cause polypharmacy, along with other medications needed to manage comorbidities(4). Polypharmacy increases the risk of drug non-compliance and causes acute rejection and poor prognosis(5). Polypharmacy has also been linked to diminished quality of life in patients who have undergone successful renal transplantation (6).

Today, the fact that it is now possible to treat many diseases has led to an increase in life expectancy and living longer with chronic diseases. As a result, the notion of quality of life has come to the forefront in evaluating treatment effectiveness (7). The assessment of quality of life is also carried out through questionnaires in which patient participation is at the forefront and has taken its place alongside physiological measures in evaluating treatment efficacy(8). Although there are many

questionnaires used for this purpose, the Kidney Disease Quality of Life Short Form (KDQOL-SF), a scale specific to renal patients, was used in our study.

Studies on polypharmacy in renal transplant patients are very limited in the literature(6). Studies in other disease groups have confirmed that polypharmacy is associated with medication adherence. Such studies are essential to draw attention to the effect of polypharmacy, which has become a significant public health problem, on the quality of life of renal transplant patients. This study aimed to assess the impact of polypharmacy on the quality of life in renal transplant patients.

### 2. Material and Method

This study included 128 patients who visited Ondokuz Mayıs University Faculty of Medicine Nephrology outpatient clinic between September 2023 and November 2023 and who agreed to participate in the study. Information form and KDQOL-SF v1.3 translated into Turkish and proven effective form were used by face-to-face interviews with the patients. The Excel spreadsheet for scoring the KDQOL-SF available on the website was used to score this questionnaire. Each section is scored between 0-100 in different sub-scores.

Blood pressure, weight and height information were obtained from the nurse interviews with the patients before the

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examination. Complete blood count, basic biochemical parameters, urine protein creatinine ratio, and medication levels on the day the questionnaire was completed were obtained from the hospital information system. Patient statements, anamnesis notes of the patients and biopsy results were taken into consideration while evaluating the etiology of CKD. Patients were evaluated for comorbidities such as diabetes mellitus, hypertension, coronary artery disease and other chronic diseases requiring regular medication. Patients with more than one disease in these defined conditions were defined as having concomitant multimorbidity.

Patients were categorized in terms of the number of drugs they used daily. Although there are various definitions of polypharmacy, patients who used  $\geq 6$  drugs previously utilized frequently in studies for polypharmacy were defined as the polypharmacy group. Patients using five or fewer drugs were considered as the non-polypharmacy group.

### 2.1. Statistical analysis

Statistical significance was determined as  $p < 0.05$ . IBM SPSS 24.0 package programme was used for data entry and analyses. In analyses, the correlation of quantitative variables with polypharmacy status was determined by the Pearson chi-square test. The conformity of continuous variables to normal distribution was evaluated by histogram graphs and Kolmogorov-Smirnov and Shapiro-Wilk tests. If the continuous variables were suitable for normal distribution, the

Student-t test was applied for the comparisons of the groups with and without polypharmacy; if the continuous variables were not suitable for normal distribution, the Mann-Whitney u test was applied for the comparisons of the groups with and without polypharmacy.

### 3. Results

Among the 128 patients in our study, 77 (60.2%) were male and 51 (39.8%) were female. Moreover, among the patients who participated in the study, 95 (74.2%) were married and 33 (25.8%) were single. The mean was  $47.8 \pm 12.8$  years. When the patients were classified according to the number of medications, 74 patients (57.8%) were grouped as polypharmacy group, and 54 patients (42.3%) were grouped as non-polypharmacy group. Age was statistically significantly higher in the polypharmacy group. When the participants were compared regarding polypharmacy status, no statistically significant result was found between gender and polypharmacy status. When the patients were compared in terms of marital status, the presence of polypharmacy was found to be statistically significantly higher in married individuals than in single individuals (Table 1).

When the study participants were evaluated in terms of the number of drugs, it was observed that the patients used an average of  $6.7 \pm 2.4$  drugs. When the participants were evaluated in terms of daily drug load, it was observed that the mean drug load was  $11 \pm 3.9$  tablets.

**Table 1.** Relationship between polypharmacy status and epidemiological data

		Polypharmacy				p
		None		Yes		
		Number	Percentage	Number	Percentage	
Gender	Male	28	36.4	49	63.6	0.101
	Female	26	51.0	25	49.0	
Marital status	Married	35	36.8	60	63.2	<b>0.038</b>
	Single	19	57.6	14	42.4	

When the participants were evaluated in terms of donor type, it was observed that 80 (62.5%) of 128 patients received renal transplantation from living donors and 48 (37.5%) from cadaveric donors. There was no statistically significant difference between polypharmacy and donor type.

The KDQOL-SF questionnaire results of the patients participating in the study were evaluated regarding polypharmacy status. Patients were evaluated under 20 subheadings, including nine under the quality of life related to renal disease and nine under the quality of life-related to general health and SF-12 components. Higher scores in the questionnaire results were evaluated to be associated with better quality of life. When the results of the patients' questionnaires were evaluated, it was found that the non-polypharmacy group had statistically significantly better

quality of life in all sub-headings. In other words, quality of life was lower in the group with polypharmacy in every subheading (Table 2).

### 4. Discussion

Polypharmacy has become a significant health problem today due to increasing life expectancy and accompanying chronic diseases. Polypharmacy is known to be an essential public health problem with an impact on quality of life(9). Renal transplant patients are also exposed to polypharmacy, particularly during the initial post-transplant period, and polypharmacy is considered to affect the quality of life and medication compliance of renal transplant patients. However, there have not been sufficient studies evaluating the impact of polypharmacy on quality of life, especially in the renal transplant group.

**Table 2.** Relationship between polypharmacy status and KDQOL-SF questionnaire parameters

	PF	Ave.	SD	Med.	Min.	Max.	p
<b>Relationship between Renal Disease and Quality of Life</b>							
Symptom problem list	None	95.2	8.0	98.9	61.4	100.0	<0,001
	Yes	87.9	11.7	89.8	38.6	100.0	
Renal disease effect	None	92.8	10.8	96.9	59.4	100.0	<0,001
	Yes	80.3	15.8	81.3	25.0	100.0	
Renal disease burden	None	75.6	22.4	81.3	6.3	100.0	<0,001
	Yes	49.7	30.7	43.8	0.0	100.0	
Labour status	None	61.1	37.2	50.0	0.0	100.0	0.001
	Yes	37.8	40.4	50.0	0.0	100.0	
Cognitive function	None	82.5	16.5	83.3	40.0	100.0	0.004
	Yes	73.7	16.9	73.3	33.3	100.0	
Quality of social interaction	None	69.3	11.7	66.7	26.7	93.3	0.029
	Yes	64.4	14.4	66.7	20.0	100.0	
Sexual function	None	84.2	16.1	87.5	50.0	100.0	0.001
	Yes	65.2	24.8	62.5	0	100.0	
Sleep	None	82.9	14.2	85.0	42.5	100.0	0.001
	Yes	74.4	16.2	72.5	2.5	100.0	
Social support	None	90.7	19.6	100.0	0.0	100.0	<0,001
	Yes	71.6	24.5	66.7	0.0	100.0	
<b>Relationship between General Health and Quality of Life</b>							
General health perception	None	27.6	4.3	30.0	20.0	30.0	<0,001
	Yes	23.2	5.0	20.0	10.0	30.0	
Physical functionality	None	87.4	18.3	94.4	11.1	100.0	<0,001
	Yes	74.5	21.5	77.8	16.7	100.0	
Physical problems	None	75.5	30.5	75.0	0.0	100.0	<0,001
	Yes	41.2	38.0	50.0	0.0	100.0	
Pain	None	93.2	14.1	100.0	22.5	100.0	<0,001
	Yes	81.9	19.7	90.0	20.0	100.0	
General health	None	73.0	21.0	80.0	15.0	100.0	<0,001
	Yes	55.0	25.7	50.0	15.0	95.0	
Emotional well-being	None	74.6	11.9	76.0	44.0	100.0	0.002
	Yes	66.2	17.5	64.0	12.0	100.0	
Emotional problems	None	84.6	32.8	100.0	0.0	100.0	<0,001
	Yes	57.7	47.2	100.0	0.0	100.0	
Social functionality	None	86.3	19.3	87.5	25.0	100.0	<0,001
	Yes	67.4	26.0	62.5	0.0	100.0	
Energy fatigue	None	70.3	16.8	75.0	30.0	100.0	0.001
	Yes	60.9	16.8	60.0	25.0	100.0	
<b>SF-12 Components</b>							
SF12 Physical	None	51.5	6.0	54.2	32.1	57.2	<0,001
	Yes	46.3	6.7	46.0	32.4	60.7	
SF12 Mental	None	50.6	7.0	52.9	31.0	62.4	<0,001
	Yes	44.5	9.6	45.5	26.0	62.5	

In our study, no significant difference was found between male and female gender in terms of the presence of polypharmacy. In a study by Schmidt et al. evaluating the burden of polypharmacy in patients with chronic kidney disease, polypharmacy was more common in females(10). In another study by Wozniak et al., in which polypharmacy was analyzed in renal transplant patients, there was no difference in the frequency of polypharmacy between male and female gender(6). There were different results in the literature

regarding the relationship between gender and polypharmacy. In our study, the frequency of polypharmacy was higher in married individuals. In a study conducted in 2021 by Balkhi et al. covering all disease groups, polypharmacy was found to be higher in married participants when all participants were evaluated. When the study was evaluated in the elderly group, no relationship was found between marital status and polypharmacy(11). In our study, since the mean age of the married group was 52±10.4 years and the mean age of the

single group was  $35.9 \pm 11.6$  years, it was interpreted that this relationship was related to age. In our study, a notable correlation was observed between age and polypharmacy. In a study conducted by Adhikari et al. in renal transplant patients, a direct correlation between age and drug burden was reported, and it was thought that this was due to comorbidities increasing with age(12). In a study conducted by Ameri et al. in a group of elderly patients, it was shown that the frequency of polypharmacy increased with age, and in the same study, it was also shown that the frequency of comorbidity increased with age(13). In our study, it was interpreted that the increasing frequency of polypharmacy with increasing age was related to the presence of multimorbidity.

In our study, it was observed that there was no significant correlation between drug levels and polypharmacy. When the literature was reviewed, no other study was found examining the relationship between drug levels and polypharmacy in renal transplant patients. Our study is the first study in the literature in this respect and further large-scale and multicentre studies on this subject will help to clarify the relationship between drug level and polypharmacy.

When the results of the KDQOL-SF questionnaire used in our study were evaluated, both general health-related quality of life parameters, renal disease-related quality of life parameters and SF-12 components were lower in patients exposed to polypharmacy. Wozniak et al. evaluated the effect of polypharmacy in renal transplant patients using the KDQOL-SF, and patients were analyzed in 3 groups according to the number of drugs: those using less than five drugs, those using between 5-9 drugs and those using more than ten drugs and each group was compared with each other. In the study conducted by Wozniak et al., physical functioning, pain, social function, energy/fatigue, burden and impact of renal disease were directly lower in patients taking at least ten medications compared to the other two groups. In other statistical studies, an inverse correlation was found between symptom/problem list, physical functioning, pain, physical problems, general health, social functioning, energy/fatigue and number of medications.

Multivariate regression analyses showed that the number of medications acted as an independent variable for physical, pain, and social functioning. In addition, it was found that drug burden and drug cost harmed quality of life. As a result, Wozniak et al. concluded that polypharmacy negatively affects quality of life in renal transplant patients through the use of the KDQOL-SF quality of life questionnaire (6). In a study published by Adjero et al. with CKD patients who were not receiving dialysis treatment, the participants' quality of life was evaluated, and the patients were evaluated in terms of physical

and mental components. The study found that polypharmacy was associated with lower quality of life in CKD patients not receiving dialysis(14). Although this study was not conducted in renal transplant patients, the relationship between polypharmacy and quality of life was shown in a CKD patient group, similar to our study.

In conclusion, polypharmacy is one of the factors that negatively affect the quality of life of renal transplant patients. Considering that renal transplantation is the most important RRT treatment that improves the quality of life of patients with CKD, improving the quality of life of patients and its follow-up is vital for patients. We believe that a multicentre study investigating the effect of polypharmacy on quality of life in renal transplant patients with more participants would give us better results.

Our study has demonstrated that polypharmacy reduces the quality of life in kidney transplant recipients. To prevent this, we recommend reviewing the medications used in every visit of kidney transplant patients to assess polypharmacy, discontinuing inappropriate medications, and evaluating the patients' quality of life at regular intervals using appropriate scales.

Our study's limitations include being conducted at a single center and not having a sufficient number of patients, despite being consistent with patient numbers reported in the literature. Additionally, patients' lack of awareness about the importance of survey studies can be considered a reason for their reluctance to participate in the study and respond to the questions.

#### **Conflict of interest**

The authors declared no conflict of interest.

#### **Funding**

No funding was used for the study.

#### **Acknowledgments**

None to declare.

#### **Authors' contributions**

Concept: F.Ç., A.K., N.A., E.T., Design: F.Ç., A.K., N.A., Data Collection or Processing: F.Ç., A.K., Analysis or Interpretation: F.Ç., A.K., Literature Search: F.Ç., A.K., E.T., Writing: F.Ç., A.K., N.A., E.T.

#### **Ethical Statement**

Approval was obtained from Ondokuz Mayıs University Clinical Research Ethics Committee, the study started. The ethics committee decision date is 24/08/2023 and the number of ethical committee decisions is 2023/172.

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