Polypharmacy and Accompanying Comorbid Conditions in Kidney Transplant Recipients: A Retrospective Study

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Abstract

Aim: Kidney transplantation improves survival and quality of life, yet post-transplant care frequently necessitates complex pharmacotherapy due to immunosuppressive regimens and management of comorbidities. This often results in polypharmacy, which is associated with increased risk of adverse outcomes. In this study, we aimed to evaluate the immunosuppressive and other medications used in kidney transplant recipients, as well as the accompanying comorbid conditions.

Methods: In this cross-sectional, multicenter study, 342 kidney transplant recipients were stratified into two groups: low-risk (≤5 medications) and moderate-to-high risk (≥6 medications) polypharmacy. Demographic, clinical, and laboratory data were analyzed to identify predictors of polypharmacy using multivariate logistic regression.

Results: Moderate-to-high polypharmacy was observed in 64.9% of patients. This group had significantly higher creatinine, blood urea nitrogen (BUN), and glucose levels, and lower eGFR and hemoglobin values (all $p < 0.05$). Hypertension, diabetes, and coronary artery disease were more common in this group ($p = 0.001$). In multivariate analysis, hypertension (OR: 4.615), proton pump inhibitor use (OR: 5.705), and allopurinol use (OR: 10.894) were independently associated with polypharmacy, while anticoagulant use was inversely associated (OR: 0.237; all $p < 0.01$).

Conclusions: Polypharmacy is prevalent among our kidney transplant recipients and is associated with impaired graft function, anemia, and higher comorbidity burden. Certain medications, particularly PPIs and allopurinol, are strong predictors of polypharmacy. These findings highlight the need for individualized medication review, deprescribing strategies, and integration of pharmacogenomics into routine care to optimize outcomes in transplant recipients.

Keywords: *Polypharmacy; kidney transplantation; comorbidities; medication management; immunosuppressive therapy*

1. Introduction

Kidney transplantation is the preferred renal replacement therapy, offering better survival and quality of life than dialysis.[1,2] However, the complexity of post-transplant care frequently results in polypharmacy, driven by immunosuppressive needs and management of comorbidities like hypertension, diabetes, and cardiovascular disease.[3,4]

Polypharmacy is commonly defined as the concurrent use of five or more medications. Hyperpolypharmacy, a more severe form, typically refers to the use of ten or more medications.[5] These thresholds, while not universally standardized, are widely cited in the literature and provide a framework for risk stratification.[6-8]

Studies report that more than two-thirds of transplant recipients are exposed to hyperpolypharmacy (≥10 medications), increasing the risk of adverse drug interactions and non-adherence.[9,10] Despite being a global concern, data on polypharmacy in Turkish transplant populations are scarce. This study presents one of the largest multicenter datasets in Turkey to examine the prevalence of polypharmacy and its clinical correlates. In particular, we

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aimed to explore independent predictors of polypharmacy using multivariate analysis, focusing on frequently prescribed medications such as PPIs and allopurinol.

2. Materials and Methods

2.1. Study Design and Setting

This was a cross-sectional study conducted at two transplant centers in Türkiye. The study period spanned from March 2016 to December 2017.

2.2. Participants

A total of 370 adult kidney transplant recipients with functioning grafts were screened. All eligible patients who attended regular follow-up visits during the study period were consecutively included to minimize selection bias. Patients were excluded if they had incomplete medical records (n = 18), experienced graft loss (n = 10), had acute kidney injury, acute or chronic infections, a history of hospitalization within the past month, malignancy, acute heart failure, acute coronary syndrome, recent medication changes, or if they declined to participate. The final study population included 342 patients who met the inclusion criteria.

2.3. Inclusion Criteria

Patients were included if they were ≥18 years old, had a functioning graft, were under regular outpatient follow-up, adhered to their prescribed medications, and had consistent physical examinations and laboratory data properly recorded.

2.4. Grouping Based on Polypharmacy Risk

Participants were stratified into two groups according to the number of medications used: those taking five or fewer medications were classified as the low-risk polypharmacy group, while those taking six or more medications were classified as the moderate-to-high-risk polypharmacy group. Polypharmacy was defined as the use of ≥6 medications, in line with previous studies on kidney transplant recipients, to ensure consistency and comparability across the literature [5,9].

2.5. Data Collection

Demographic, clinical, and laboratory data were retrospectively collected from hospital records. All laboratory tests were performed in accredited hospital laboratories using standardized protocols and identical or equivalent autoanalyzers across both centers to ensure measurement consistency and minimize inter-center variability.

Under the heading of anticoagulant therapy, we included both antiplatelet agents (e.g., aspirin, clopidogrel) and oral anticoagulants (e.g., warfarin, novel oral anticoagulants [NOACs]). In our study, only antiplatelet therapy was used in the low-risk polypharmacy group, whereas oral anticoagulants were rarely used and exclusively in the moderate-to-high risk group.

2.6. Bias Considerations

To reduce selection bias, all eligible patients were consecutively included. However, as a retrospective study, potential information bias due to incomplete documentation or unrecorded over-the-counter medication use could not be fully excluded.

2.7. Target Blood Levels for Immunosuppressive Medications

Target blood levels for immunosuppressive medications were as follows: Tacrolimus C0: 7–10 ng/mL during the first month and 3–7 ng/mL thereafter; Cyclosporine C0: 200–300 ng/mL during months 1–3 and 50–150 ng/mL subsequently; Cyclosporine C2: 800–1000 ng/mL during months 1–3 and 400–600 ng/mL thereafter; Sirolimus: 4–6 ng/mL; Everolimus: 5–7 ng/mL.

2.8. Sample Size and Power Analysis

Prior to data analysis, a power analysis was conducted using G*Power to estimate the required sample size. To detect a medium effect size (Cohen's d = 0.5) with 80% power and a significance level of $\alpha = 0.05$ in between-group comparisons, a minimum of 128 participants (64 per group) was deemed necessary. The final sample size of 342 patients exceeded this requirement, indicating sufficient statistical power to detect clinically meaningful differences.

2.9. Statistical Analysis

Descriptive statistics were used to summarize demographic, clinical, and laboratory characteristics. Continuous variables were presented as mean ± standard deviation or median (interquartile range), depending on the distribution. Categorical variables were expressed as frequencies and percentages. The Shapiro–Wilk test was used to assess the normality of data distribution. For group comparisons: Independent t-tests were used for normally distributed continuous variables. Mann–Whitney U tests were applied to non-normally distributed variables. Chi-square tests or Fisher's exact tests were used for categorical variables.

To evaluate factors associated with polypharmacy, logistic regression analysis was performed using the enter method. Variables with a p-value <0.05 in univariate analysis were included in the multivariate regression model. Results were reported as odds ratios (ORs) with 95% confidence intervals (CIs). A p-value <0.05 was considered statistically significant for all analyses. Potential confounders such as age, gender, comorbidities (e.g., hypertension, diabetes mellitus, and coronary artery disease), and renal function parameters (e.g., creatinine, eGFR) were included in the multivariate analysis based on clinical relevance and prior literature. Diagnoses of comorbidities were based on physician-documented diagnoses and/or the documented use of corresponding medications in patient records. No subgroup, interaction, or sensitivity analyses were performed in this study. The primary analysis relied on multivariate logistic regression including clinically relevant covariates. Cases with missing data were excluded from the relevant analyses (complete-case analysis). The proportion of missing data was minimal and did not affect the overall validity of the results. As all eligible patients were consecutively included in the study, no weighting or sampling-adjusted analytical methods were necessary. No sensitivity analyses were performed.

All statistical analyses were performed using SPSS 18.0 for Windows (SPSS Inc., Chicago, IL, USA). Data from the two centers were pooled for analysis, and no significant inter-center differences were detected that could influence the results.

3. Results

Table 1 shows the demographic characteristics of the study groups. The mean age was 41.38 ± 12.37 years in the low-risk group and 43.41 ± 12.96 years in the moderate-to-high risk group (p=0.161). No statistically significant differences were observed between the groups regarding gender, donor source, donor gender, or mean age. The mean post-transplant duration was shorter in the moderate-to-high risk group compared to the low-risk group (5.56 ± 4.29 vs. 7.45 ± 5.18 years, p=0.001).

Table 2 presents the comparison of laboratory parameters between the groups. Patients in the moderate-to-high risk group had higher creatinine (1.39 ± 0.7 mg/dL vs. 1.24 ± 0.61 mg/dL, p=0.024), BUN (21.12 ± 13.04 mg/dL vs. 17.13 ± 10.81 mg/dL, p=0.001), and glucose levels (106.28 ± 50.55 mg/dL vs. 96.59 ± 27.13 mg/dL, p=0.010). Conversely, e-GFR (71.6 ± 28.68 ml/min. vs. 77.98 ± 25.75 ml/min., p=0.043) and hemoglobin levels (13.3 ± 2.09 g/dL vs. 13.8 ± 1.89 g/dL, p=0.027) were lower in the moderate-to-high risk group.

Table 1

Demographic Data

		Polypharmacy Groups		P
		Low Risk Polypharmacy ≤5 medications (n: 120)	Medium-High Risk Polypharmacy ≥6 medications (n: 222)	
Gender of Recipient	Female	47 (39.2%)	78 (35.1%)	0.460
	Male	73 (60.8%)	144 (64.9%)	
Type of Donation	Living Related Donor	86 (72.3%)	172 (77.4%)	0.571
	Kidney Paired Donation	10 (8.4%)	16 (7.2%)	
	Deceased Donor	24 (9.3%)	34 (15.4%)	
Gender of Donor	Female	54 (45.3%)	117 (53.8%)	0.201
	Male	66 (54.7%)	105 (46.2%)	
Age		41.38±12.37	43.41±12.96	0.161
Number of Drugs		4.40±0.78	7.07±1.34	**0.001**
Duration of Kidney Transplantation (years)		7.45±5.18	5.56±4.29	**0.001**

Table 2

Comparison of polypharmacy groups with laboratory data

	Polypharmacy Groups		P
	Low Risk Polypharmacy ≤5 medications (n: 120)	Medium-High Risk Polypharmacy ≥6 medications (n: 222)	
Creatinine (mg/dL)	1.24±0.61 (1.09)	1.39±0.7 (1,21)	**0.024***
e-GFR (ml/min)	77.98±25.75	71.6±28.68	**0.043**
Glucose (mg/dl)	96.59±27.13 (89)	106.28±50.55 (94)	**0.010***
White Blood Cell Count ($x10^9$/L)	9061.58±3314.78 (8395)	9214.36±2801.39 (9205)	0.291*
Hemoglobin (g/dL)	13.8±1.89	13.3±2.09	**0.027**
Hematocrit (%)	42.78±5.74	41.61±6.33	0.094
Platelets ($x10^9$/L)	258145.83±76960.36	258754.55±75374.76	0.944
AST (u/L)	20.19±8.65 (19)	19.41±10.19 (18)	0.065*
ALT (u/L)	21.89±14.03 (18.5)	23.87±27.06 (18)	0.791*
BUN (mg/dL)	17.13±10.81 (14)	21.12±13.04 (17)	**0.001***
Magnesium (mg/dL)	4.39±21.94	1.81±0.23	0.323
Sodium (mg/dL)	137.07±3.32	137.59±2.79	0.129
Potassium (mg/dL)	4.27±0.68	4.28±0.54	0.860
Calcium (mg/dL)	9.58±0.62 (9.6)	9.48±0.73 (9.5)	0.114*
Phosphorus (mg/dL)	3.33±0.94	3.42±0.75	0.311
Free T3 (pmol/L)	4.03±0.83	3.73±0.61	0.070
Free T4 (pmol/L)	0.87±0.1 (0.88)	0.98±0.33 (0.94)	0.056*
TSH (mIU/L)	2.13±1.45 (1.64)	1.9±1.3 (1.76)	0.462*

Abbreviations: e-GFR: *estimated glomerular filtration rate,* ***AST:*** *aspartate aminotransferase,* ***ALT:*** *alanine aminotransferase,* ***BUN:*** *Blood urine nitrogen,* ***TSH:*** *Thyroid stimulating hormone*

**Due to the non-normal distribution of the data, medians were compared using the Mann-Whitney U test, with median values presented in parentheses.*

Table 3

Comparison of polypharmacy groups in terms of additional factors

		Polypharmacy Groups		P
		Low Risk Polypharmacy ≤5 medications (n: 120)	Medium-High Risk Polypharmacy ≥6 medications (n: 222)	
Proteinuria (mg/dL)	<150mg	86 (74.8%)	136 (63.3%)	0.092
	150-1000mg	19 (16.5%)	40 (18.6%)	
	1000-3500mg	7 (6.1%)	23 (10.7%)	
	>3500mg	3 (2.6%)	16 (7.4%)	
Hematuria	>5 HPF	11 (9.6%)	22 (10.4%)	0.888
	<5 HPF	102 (89.5%)	189 (89.2%)	
Pyuria	<5 HPF	92 (80.7%)	184 (86.8%)	0.146
	>5 HPF	22 (19.3%)	28 (13.2%)	
Immunosuppressive Drug Levels	Within target range	79 (69.3%)	126 (60.3%)	0.134
	Below Target Range	28 (24.6%)	57 (27.3%)	
	Above Target Range	7 (6.1%)	26 (12.4%)	
Hypertension	Yes	66 (55%)	176 (79.3%)	**0.001**
	No	54 (45%)	46 (20.7%)	
Diabetes Mellitus	Yes	3 (2.5%)	50 (22.6%)	**0.001**
	No	115 (%97,5)	171 (77.4%)	
Coronary artery disease	Yes	3 (2.5%)	34 (15.4%)	**0.001**
	No	115 (97.5%)	187 (84.6%)	
PPI therapy	Yes	12 (10%)	77 (34.7%)	**0.001**
	No	108 (90%)	145 (65.3%)	
H2 Receptor Blocker therapy	Yes	47 (39.5%)	79 (35.6%)	0.476
	No	72 (60.5%)	143 (64.4%)	
Anti-hypertensive therapy	ACEI or ARB	14 (11.7%)	9 (4.1%)	**0.001**
	ACEI or ARB + thiazide	8 (6.7%)	33 (14.9%)	
	Beta blockers	14 (11.7%)	27 (12.2%)	
	CCB	25 (20.8%)	35 (15.8%)	
	Alpha Blocker	0 (0%)	3 (1.4%)	
	None	50 (41.7%)	49 (22.1%)	
	Alpha + Beta blockers	0 (0%)	7 (3.2%)	
	Beta blockers + CCB	7 (5.8%)	50 (%22,5)	
	Furosemide	1 (0.8%)	4 (1.8%)	
	Alpha Blocker + CCB	1 (0.8%)	5 (2.3%)	
Anti-hyperlipidemic therapy	Statins	2 (1.7%)	16 (7.2%)	**0.046**
	Fibrats	2 (1.7%)	2 (0.9%)	
	No	116 (96.7%)	203 (91.9%)	
Oral antidiabetic drug therapy	Yes	1 (0.8%)	20 (9%)	**0.003**
	No	119 (99.2%)	202 (91%)	
Insulin therapy	Yes	2 (1.7%)	27 (12.2%)	**0.001**
	No	118 (98.3%)	195 (87.8%)	
Anti-coagulant therapy	Antiplatelet therapy	17 (14.2%)	79 (36.1%)	**0.001**
	Oral anticoagulants	0 (0%)	5 (2.3%)	
	No	103 (85.8%)	134 (61.2%)	

Continuation of Table 3

Immunosuppressive Regimen	Tac+MMF+Steroid	55 (45.8%)	135 (60.8%)	**0.006**
	Cyc+MMF+Steroid	6 (5%)	21 (9.5%)	
	Cyc + AZA + Steroid	3 (2.5%)	7 (3.2%)	
	Tac + Eve + Steroid	2 (1.7%)	5 (2.3%)	
	Tac + AZA + Steroid	17 (14.2%)	20 (9%)	
	Tac + Eve + Steroid	2 (1.7%)	4 (1.8%)	
	Sir + MMF + Steroid	2 (1.7%)	1 (0.5%)	
	Eve + MMF + Steroid	0 (0%)	2 (0.9%)	
	Tac + Steroid	11 (9.2%)	9 (4.1%)	
	Cyc + Steroid	3 (2.5%)	10 (4.5%)	
	Tac + MMF	7 (5.8%)	2 (0.9%)	
	Tac + Sir	2 (1.7%)	0 (0%)	
	Tac + AZA	4 (3.3%)	3 (1.4%)	
	Cyc	1 (0.8%)	0 (0%)	
	Tac	5 (4.2%)	3 (1.4%)	
Allopurinol therapy	Yes	2 (1.7%)	19 (8.6%)	**0.011**
	No	118 (98.3%)	203 (91.4%)	

Abbreviations: HPF: *High power field,* ***ACEI:*** *Angiotensin converting enzyme inhibitör,* ***ARB:*** *Angiotensin receptor blocker,* ***TAC:*** *Tacrolimus,* ***MMF:*** *Mycophenoplate mofetile,* ***AZA:*** *azathiopurin,* ***CYC:*** *Cyclosporin,* ***EVE****: Everolimus,* ***Sir:*** *Sirolimus,* ***CCB:*** *Calcium channel blockers*

Table 4

Logistic regression analysis for variables of polypharmacy risk

Variable	B	p	Exp(B)	95% C.I.for EXP(B)	
				Lower	Upper
Hypertension	1,529	**0,001**	4,615	2,473	8,612
Diabetes Mellitus	3,265	0,234	26,170	0,121	5665,311
Coronary Artery Disease	0,421	0,587	1,523	0,334	6,948
Proton pump inhibitor therapy	1,741	**0,001**	5,705	2,701	12,050
Anti-hyperlipidemic drug therapy	0,167	0,807	1,182	0,310	4,500
Oral anti-diabetic drug therapy	-0,987	0,717	0,373	0,002	76,765
Insulin therapy	-0,771	0,777	0,462	0,002	95,696
Allopurinol therapy	2,388	**0,004**	10,894	2,184	54,347
Anti-coagulant therapy	-1,439	**0,001**	0,237	0,120	0,469

Abbreviations: e-GFR: *estimated glomerular filtration rate*

Table 3 highlights the prevalence of comorbidities and medication use between the groups. The prevalence of hypertension (79.3% vs. 55%, p=0.001), diabetes mellitus (22.6% vs. 2.5%, p=0.001), and coronary artery disease (15.4% vs. 2.5%, p=0.001) was significantly higher in the moderate-to-high risk group compared to the low-risk group. Additionally, the moderate-to-high risk group had higher rates of PPI therapy (34.7% vs. 10%, p=0.001), allopurinol therapy (8.6% vs. 1.7%, p=0.011), and anticoagulant therapy (38.8% vs. 14.2%, p=0.001).

Table 4 summarizes the logistic regression analysis results. Logistic regression analysis identified significant predictors of polypharmacy. The presence of hypertension (OR: 4.615, p=0.001), PPI use (OR: 5.705, p=0.001), and allopurinol use (OR: 10.894, p=0.004) were independently associated with moderate-to-high risk polypharmacy, while anticoagulant use was inversely associated (OR: 0.237, p=0.001). While diabetes mellitus and coronary artery disease were more prevalent in the moderate-to-high risk group, these factors did not reach statistical significance in the regression model.

4. Discussion

This multicenter study underscores the high prevalence of moderate-to-high polypharmacy in Turkish kidney transplant recipients and its significant association with impaired renal function, anemia, and a heavier comorbidity burden. These findings

align with previous reports indicating that kidney transplant patients frequently require complex pharmacological regimens to manage both immunosuppression and multiple comorbid conditions such as hypertension, diabetes, and cardiovascular disease.[2,3,7]

While the definition of polypharmacy varies across studies, thresholds such as ≥5, ≥6, or ≥10 medications are commonly used. We adopted the ≥6 threshold, consistent with previous work in transplant populations[4] which facilitates early identification of at-risk patients. In line with findings from Kosoku et al., our study shows that higher medication burden is associated with clinical frailty and adverse laboratory parameters.[5]

Our results revealed that patients in the moderate-to-high polypharmacy group had significantly higher creatinine and BUN levels and lower eGFR compared to the low-risk group. These findings corroborate the work of Kang and Hong, who showed that polypharmacy increased the risk of kidney dysfunction in older populations[11] and support the recent meta-analysis by Oosting et al. linking polypharmacy to worse outcomes in chronic kidney disease (CKD).[8] However, Harhay et al. pointed out the need to account for confounding variables such as frailty and medication types, which could alter the interpretation of this association.[3]

Although diabetes mellitus and coronary artery disease were more prevalent in the high-risk group, they were not independently associated with polypharmacy risk in the multivariate analysis. This suggests potential confounding by other variables and indicates that their impact should be interpreted cautiously. A similar observation was reported by Harhay et al., who emphasized that comorbidities such as diabetes may not directly drive polypharmacy when adjusted for broader clinical context including frailty, functional capacity, and immunosuppressive needs.[3]

Interestingly, PPI and allopurinol use were strongly associated with polypharmacy in our cohort. Our findings regarding the frequent use of proton pump inhibitors in kidney transplant recipients are consistent with previous reports demonstrating high PPI prescription rates in patients with chronic kidney disease, both with and without kidney replacement therapy.[12] These medications, although often clinically justified, carry well-documented risks. PPI use has been associated with adverse outcomes such as hypomagnesemia, infections, and renal injury, especially with long-term use.[13] Allopurinol, while effective for hyperuricemia, requires careful dosing in transplant patients due to altered pharmacokinetics and nephrotoxicity risk.[14] Similarly, the association between allopurinol use and polypharmacy in our cohort aligns with prior evidence highlighting the common use of urate-lowering therapy, particularly allopurinol, among solid-organ transplant recipients[15] Our findings also support earlier reports emphasizing the importance of regular medication review to identify potential drug-related problems in transplant populations.[16] These findings likely reflect prescribing practices in patients with multiple comorbidities rather than indicating causality.

In the context of polypharmacy, potential drug-drug and drug-food interactions represent critical but often underrecognized contributors to adverse clinical outcomes. Kidney transplant recipients are particularly vulnerable due to the narrow therapeutic index of immunosuppressive agents and the frequent use of multiple medications with overlapping metabolic pathways. For instance, proton pump inhibitors and certain antibiotics may alter the absorption or metabolism of calcineurin inhibitors, leading to subtherapeutic or toxic blood levels.[12] Likewise, dietary components such as grapefruit juice can significantly affect cyclosporine and tacrolimus bioavailability.[13] Although our study did not systematically assess interaction profiles, the high prevalence of polypharmacy in this cohort suggests a considerable risk of such interactions. Gago-Sánchez et al. previously highlighted the real clinical impact of these interactions in transplant recipients, especially concerning immunosuppressive drugs.[17,18] Future studies should incorporate pharmacokinetic and pharmacogenomic analyses to better understand the clinical implications of drug-drug and drug-food interactions in this population.

Although unadjusted analyses suggested higher anticoagulant use in patients with moderate-to-high polypharmacy, the multivariate model revealed an inverse association after adjusting for comorbidities and concomitant medications. A similar observation was made by Gago-Sánchez et al., who highlighted that transplant patients on immunosuppressants benefit from active management of drug interactions[15] Mechanistically, polypharmacy may affect renal function through nephrotoxic drug interactions, immunosuppressant level fluctuations, or decreased adherence. Interestingly, the negative association with anticoagulant use could indicate that these patients are under stricter clinical surveillance, involving closer follow-up and more cautious prescribing practices, thereby potentially minimizing unnecessary polypharmacy.

Anemia, often multifactorial in transplant recipients, was more common in the moderate-to-high polypharmacy group. This may stem from impaired erythropoiesis due to lower eGFR, PPI-associated iron or vitamin B12 malabsorption, and possible chronic GI bleeding, particularly in those using anticoagulants. Sakamoto et al. reported a similar relationship in cardiovascular outpatients, linking polypharmacy with accelerated renal decline and anemia.[19]

Only 6.4% of our patients had hyperpolypharmacy (≥10 medications), which is substantially lower than the 66% reported by Atić et al. in a similar transplant cohort.[9] This disparity likely reflects variations in study design, medication definitions, and data collection periods.

We also observed that patients in the moderate-to-high polypharmacy group had shorter post-transplant durations. This could indicate that more recent recipients are exposed to higher pharmacological burdens, consistent with the post-transplant period being one of intense medication use.[12] However, this finding may also reflect worse graft outcomes, a hypothesis that warrants longitudinal validation. While the exact mechanisms underlying this association remain unclear, potential contributors include increased nephrotoxicity, poorer adherence to immunosuppressive regimens, and greater susceptibility to infections or cardiovascular complications. However, the observed association may partly reflect the higher burden of comorbid conditions and intensive pharmacotherapy, particularly during the early post-transplant period.

Although our study did not directly evaluate deprescribing practices, the findings highlight the complexity and burden of pharmacotherapy in kidney transplant recipients. These observations support the rationale for implementing deprescribing strategies, individualized medication review, patient education, and therapeutic drug monitoring in clinical practice. A recent meta-analysis by Quek et al. demonstrated that deprescribing in older adults was associated with improved survival and reduced hospitalization.[20] Building on these insights, pharmacogenomic-guided therapy has been proposed as a promising tool to optimize immunosuppressant use and minimize drug-related toxicity in transplant recipients.[16] Though direct evidence in transplant populations remains limited, integrating these strategies into post-transplant care may offer substantial clinical benefits.

While this study provides valuable insights into the prevalence and implications of polypharmacy in kidney transplant recipients, several limitations warrant consideration. First, the retrospective design and reliance on hospital records may have introduced information bias, particularly regarding medication adherence and the use of over-the-counter drugs. Second, the study did not assess the

impact of polypharmacy on specific outcomes such as hospitalization rates, quality of life, or healthcare costs, which could provide a more comprehensive understanding of its consequences. The retrospective nature of the study inherently limits causal inference. Although immunosuppressants and antihyperlipidemic agents used in transplant recipients may affect hepatic and lipid metabolism, these data were not uniformly available in our dataset. Due to the retrospective nature of the study, certain key data such as the duration of concomitant medication use, the severity and duration of comorbidities, and the exact timing of laboratory measurements could not be consistently retrieved. This limitation restricts the ability to assess temporal or dose-dependent relationships. The study was limited to patients transplanted between 2016 and 2017 due to the completeness and standardization of data during that period. Although this may affect the contemporaneity of our results, we believe the findings still reflect ongoing clinical challenges related to polypharmacy in transplant populations. Future studies should be designed to incorporate these variables and include longitudinal monitoring with more recent data to better elucidate the clinical, metabolic, and pharmacological implications of polypharmacy in transplant recipients. Another limitation of our study is that over-the-counter and undocumented medications may not have been fully captured in our dataset, potentially leading to underestimation of the true prevalence of polypharmacy. These limitations may have influenced the observed associations in either direction, and the lack of appropriateness data may have led to overestimation of polypharmacy prevalence.

5. Conclusion

Polypharmacy is highly prevalent among kidney transplant recipients and is associated with impaired renal function, anemia, and a greater comorbidity burden. The use of proton pump inhibitors (PPIs) and allopurinol were strong independent predictors of polypharmacy, whereas anticoagulant use was inversely associated, possibly reflecting closer monitoring and structured prescribing in these patients. These results highlight the need for individualized medication review, deprescribing strategies, and pharmacogenomic integration in transplant care to reduce unnecessary drug burden and improve outcomes.

Statement of ethics

Ethical approval for the study was obtained from the Ethics Committee of Çukurova University (approval date: March 4, 2016; decision no: 51). The study was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants.

genAI

No artificial intelligence-based tools or generative AI technologies were used in this study. The entire content of the manuscript was originally prepared, reviewed, and approved by both authors.

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Availability of data and materials

This Data and materials are available to the researchers.

Author contributions

Both authors contributed equally to the article. Both authors read and approved the final manuscript.

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